WEST Search History

DATE: Monday, June 24, 2002

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR			
L7	L6 and @ad<19981226	11	L7
L6	(HLA adj E) and (nk or CD94$9)	17	L6
L5	L3 and (HLA adj E)	3	L5
L4	L3 and HLAE	0	L4
L3	L2 and (nk or CD94$9)	70	L3
L2	(Braud)[IN] OR (Allan) or (ogg)[in] or (ocallaghan)[in] or (mcmichael)[in]	32981	L2
L1	(Braud)[IN] OR (Allan)	32236	L1

END OF SEARCH HISTORY

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 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  Jan 25  BLAST(R) searching in REGISTRY available in STN on the Web
 NEWS  3  Jan 29  FSTA has been reloaded and moves to weekly updates
 NEWS  4  Feb 01  DKILIT now produced by FIZ Karlsruhe and has a new update
                  frequency
 NEWS  5  Feb 19  Access via Tymnet and SprintNet Eliminated Effective 3/31/02
 NEWS  6  Mar 08  Gene Names now available in BIOSIS
 NEWS  7  Mar 22  TOXLIT no longer available
 NEWS  8  Mar 22  TRCTHERMO no longer available
 NEWS  9  Mar 28  US Provisional Priorities searched with P in CA/CAplus
                  and USPATFULL
 NEWS 10  Mar 28  LIPINSKI/CALC added for property searching in REGISTRY
 NEWS 11  Apr 02  PAPERCHEM no longer available on STN.  Use PAPERCHEM2 instead.
 NEWS 12  Apr 08  "Ask CAS" for self-help around the clock
 NEWS 13  Apr 09  BEILSTEIN: Reload and Implementation of a New Subject Area
 NEWS 14  Apr 09  ZDB will be removed from STN
 NEWS 15  Apr 19  US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
 NEWS 16  Apr 22  Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
 NEWS 17  Apr 22  BIOSIS Gene Names now available in TOXCENTER
 NEWS 18  Apr 22  Federal Research in Progress (FEDRIP) now available
 NEWS 19  Jun 03  New e-mail delivery for search results now available
 NEWS 20  Jun 10  MEDLINE Reload
 NEWS 21  Jun 10  PCTFULL has been reloaded

 NEWS EXPRESS  February 1 CURRENT WINDOWS VERSION IS V6.0d,
               CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
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                                                   ENTRY    SESSION
FULL ESTIMATED COST                                 0.21       0.21

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=> s Braud V?/au or Allan D?/au or Ogg G?/au or OCallaghan C?/au or Mcmichael A?/au
L1         3511 BRAUD V?/AU OR ALLAN D?/AU OR OGG G?/AU OR OCALLAGHAN C?/AU OR
                MCMICHAEL A?/AU

=> s l3 and (nk?)
L3 NOT FOUND
The L-number entered could not be found.  To see the definition
of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).

=> s l2 and (nk?)
L2 NOT FOUND
The L-number entered could not be found.  To see the definition
of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).

=> s l1 and (nk?)
L2           47 L1 AND (NK?)

=> s l2 and (HLA (1N) E)
L3           35 L2 AND (HLA (1N) E)

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4           14 DUP REM L3 (21 DUPLICATES REMOVED)

=> dis l4 1-14 ibib abs kwic

L4   ANSWER 1 OF 14     MEDLINE                          DUPLICATE 1
ACCESSION NUMBER:   2002292488     IN-PROCESS
DOCUMENT NUMBER:    22028985   PubMed ID: 12032324
TITLE:              UL40-mediated NK evasion during productive
```

infection with human cytomegalovirus.
AUTHOR: Wang Eddie C Y; McSharry Brian; Retiere Christelle; Tomasec Peter; Williams Sheila; Borysiewicz Leszek K; **Braud Veronique M**; Wilkinson Gavin W G
CORPORATE SOURCE: Section of Infection and Immunity, University of Wales College of Medicine, Tenovus Building, Heath Park, Cardiff CF14 4XX, United Kingdom.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2002 May 28) 99 (11) 7570-5. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20020529
Last Updated on STN: 20020529

AB Human cytomegalovirus (HCMV) exploits a range of strategies to evade and modulate the immune response. Its capacity to down-regulate MHC I expression was anticipated to render infected cells vulnerable to natural killer (**NK**) attack. Kinetic analysis revealed that during productive infection, HCMV strain AD169 first enhanced and then inhibited lysis of primary skin fibroblasts by a CD94/**NKG2A**(+) **NKG2D**(+)ILT2(+) **NK** line. The inhibition of cytotoxicity against strain AD169-infected fibroblasts was abolished by prior treatment of targets or effectors with anti-MHC I and anti-CD94 monoclonal antibodies, respectively, implying a CD94/**HLA-E** -dependent mechanism. An HCMV strain AD169, UL40 deletion mutant could not inhibit CD94/**NKG2A**(+) **NK** killing against skin fibroblasts. The contribution of UL40 to evasion of primary **NK** cells then was tested in a system where targets and effectors were MHC-matched. Primary **NK** cells activated with IFNalpha as well as cultured primary **NK** cell lines showed increased killing against DeltaUL40-infected fibroblasts compared with AD169-infected targets. This effect was abrogated by depletion of CD94(+) cells. These findings demonstrate that HCMV encodes a mechanism of evasion specifically targeted against a proportion of CD94(+) **NK** cells and show that this system functions during a productive infection.

TI UL40-mediated **NK** evasion during productive infection with human cytomegalovirus.

AU Wang Eddie C Y; McSharry Brian; Retiere Christelle; Tomasec Peter; Williams Sheila; Borysiewicz Leszek K; **Braud Veronique M**; Wilkinson Gavin W G

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L4 ANSWER 2 OF 14 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2002187376 MEDLINE
DOCUMENT NUMBER: 21916945 PubMed ID: 11920559
TITLE: Human T cell receptor-mediated recognition of **HLA-E**.
AUTHOR: Garcia Pilar; Llano Manuel; de Heredia Agustin B; Willberg Christian B; Caparros Esther; Aparicio Pedro; **Braud Veronique M**; Lopez-Botet Miguel
CORPORATE SOURCE: DCEXS (Inmunologia), Universitat Pompeu Fabra, Barcelona, Spain.
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (2002 Apr) 32 (4) 936-44. Journal code: 1273201. ISSN: 0014-2980.
PUB. COUNTRY: Germany: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020403
Last Updated on STN: 20020522
Entered Medline: 20020520

AB The **HLA-E** class Ib molecule presents hydrophobic peptides derived from the leader sequences of other class I molecules, constituting the ligands for CD94/**NKG2** lectin-like receptors. Along the course of our studies on human CD94+ T cells, we characterized an alpha beta CD8+CD94/**NKG2C+** CTL clone (K14). In cytolytic assays against the murine TAP-deficient RMA-S cells transfected with human beta2 microglobulin and **HLA-E** (RMA-S/**HLA-E**), loaded with different synthetic peptides, K14 displayed a pattern of specific recognition distinct to that observed in CD94/**NKG2C+** **NK** clones tested in parallel. RMA-S/**HLA-E** cells loaded with some but not all HLA class I leader sequence peptides were efficiently recognized by K14 but not by CD94/**NKG2C** clones, andvice versa. Remarkably, K14 also reacted with **HLA-E** loaded with a peptide derived from the BZLF-1 Epstein-Barr virus protein. Anti-CD94 mAb did not prevent K14 cytotoxicity against RMA-S/**HLA-E** cells, whereas incubation with anti-clonotypic mAb specific for the K14 TCR markedly inhibited lysis. Soluble **HLA-E** tetramers refolded with different peptides (i.e. VMAPRTVLL, VMAPRTLIL, VMAPRTLFL) specifically stained K14 cells. **HLA-E** tetramer binding was minimally reduced by pretreatment with anti-CD94 mAb alone, but was completely prevented in combination with anti-clonotypic mAb. Altogether, the data unequivocally imply the generation of human T cells potentially recognizing through the alpha beta TCR **HLA-E** molecules that bind to class I- and virus-derived peptides.

TI Human T cell receptor-mediated recognition of **HLA-E**.

AU Garcia Pilar; Llano Manuel; de Heredia Agustin B; Willberg Christian B; Caparros Esther; Aparicio Pedro; **Braud Veronique M**; Lopez-Botet Miguel

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CN . . (BZLF1 protein); 0 (Biopolymers); 0 (DNA-Binding Proteins); 0 (HLA Antigens); 0 (HLA-A Antigens); 0 (HLA-B Antigens); 0 (HLA-C Antigens); 0 (**HLA-E** antigen); 0 (Histocompatibility Antigens Class I); 0 (Membrane Glycoproteins); 0 (Peptide Fragments); 0 (Protein Sorting Signals); 0 (Receptors, Antigen, T-Cell,. . .

L4 ANSWER 3 OF 14 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2001669020 MEDLINE
DOCUMENT NUMBER: 21571709 PubMed ID: 11714810
TITLE: Intramembrane proteolysis of signal peptides: an essential step in the generation of **HLA-E** epitopes.
AUTHOR: Lemberg M K; Bland F A; Weihofen A; **Braud V M**; Martoglio B
CORPORATE SOURCE: Institute of Biochemistry, Swiss Federal Institute of Technology (Eidgenossiche Technische Hochschule), Zurich, Switzerland.
SOURCE: JOURNAL OF IMMUNOLOGY, (2001 Dec 1) 167 (11) 6441-6. Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011121
Last Updated on STN: 20020124
Entered Medline: 20020102

AB Signal sequences of human MHC class I molecules are a unique source of epitopes for newly synthesized nonclassical **HLA-E** molecules. Binding of such conserved peptides to **HLA-E** induces its cell surface expression and protects cells from **NK** cell attack. After cleavage from the pre-protein, we show that the liberated MHC class I signal peptide is further processed by signal peptide peptidase in the hydrophobic, membrane-spanning region. This cut is essential for the release of the **HLA-E** epitope-containing fragment from the lipid bilayer and its subsequent transport into the lumen of the endoplasmic reticulum via the TAP.

TI Intramembrane proteolysis of signal peptides: an essential step in the generation of **HLA-E** epitopes.

AU Lemberg M K; Bland F A; Weihofen A; **Braud V M**; Martoglio B

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CN 0 (ATP-Binding Cassette Transporters); 0 (Epitopes); 0 (HLA Antigens); 0 (HLA-A 0301 antigen); 0 (HLA-A Antigens); 0 (**HLA-E** antigen); 0 (Histocompatibility Antigens Class I); 0 (Membrane Proteins); 0 (Peptide Fragments); 0 (Protein Precursors); 0 (Protein Sorting Signals); 0. . .

L4 ANSWER 4 OF 14 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2000386466 MEDLINE
DOCUMENT NUMBER: 20354863 PubMed ID: 10898498
TITLE: **HLA-E** is expressed on trophoblast and interacts with CD94/**NKG2** receptors on decidual **NK** cells.
AUTHOR: King A; **Allan D S**; Bowen M; Powis S J; Joseph S; Verma S; Hiby S E; **McMichael A J**; Loke Y W; **Braud V M**
CORPORATE SOURCE: Department of Pathology, University of Cambridge.. akk27@cam.ac.uk
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (2000 Jun) 30 (6) 1623-31. Journal code: 1273201. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000818
Last Updated on STN: 20000818
Entered Medline: 20000809

AB Non-classical MHC class I molecule **HLA-E** is the ligand for CD94/**NKG2** **NK** cell receptors. Surface expression of **HLA-E** requires binding of specific HLA class I leader sequences. The uterine mucosa in early pregnancy (decidua) is infiltrated by large numbers of **NK** cells, which are closely associated with placental trophoblast cells. In this study we demonstrate that trophoblast cells express **HLA-E** on their cell surface in addition to the previously reported expression of HLA-G and HLA-C. Furthermore, we show that the vast majority of decidual **NK** cells bind to **HLA-E** tetrameric complexes and this binding is inhibited

by mAb to CD94. Thus, recognition of fetal **HLA-E** by decidual **NK** cells may play a key role in regulation of placentation. The functional consequences of decidual **NK** cell interaction were investigated in cytotoxicity assays using polyclonal decidual **NK** cells. The overall effect of CD94/**NKG2** interaction with **HLA-E** is inhibition of cytotoxicity by decidual **NK** cells. However, since decidual **NK** cells are unable to kill trophoblast even in the presence of mAb to MHC class I molecules and **NK** cell receptors, **HLA-E** interaction with CD94/**NKG2** receptors may regulate other functions besides cytolysis during implantation.

TI **HLA-E** is expressed on trophoblast and interacts with CD94/**NKG2** receptors on decidual **NK** cells.

AU King A; **Allan D S**; Bowen M; Powis S J; Joseph S; Verma S; Hiby S E; **McMichael A J**; Loke Y W; **Braud V M**

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CN 0 (Antigens, CD); 0 (HLA Antigens); 0 (HLA-C Antigens); 0 (**HLA-E** antigen); 0 (HLA-G antigen); 0 (Histocompatibility Antigens Class I); 0 (Ligands); 0 (Membrane Glycoproteins); 0 (**NKG2** protein); 0 (Receptors, Immunologic); 0 (antigen CD94)

L4 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 5

ACCESSION NUMBER: 2000:118749 CAPLUS

DOCUMENT NUMBER: 132:292398

TITLE: Surface expression of **HLA-E**, an inhibitor of natural killer cells, enhanced by human cytomegalovirus gpUL40

AUTHOR(S): Tomasec, Peter; **Braud, Veronique M.**; Rickards, Carole; Powell, Martin B.; McSharry, Brian P.; Gadola, Stephan; Cerundolo, Vincenzo; Borysiewicz, Leszek K.; **McMichael, Andrew J.**; Wilkinson, Gavin W. G.

CORPORATE SOURCE: Department of Medicine, University of Wales College of Medicine, Cardiff, CF14 4XN, UK

SOURCE: Science (Washington, D. C.) (2000), 287(5455), 1031-1033
CODEN: SCIEAS; ISSN: 0036-8075

PUBLISHER: American Association for the Advancement of Science

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The nonclassical major histocompatibility complex (MHC) class I mol. **HLA-E** inhibits natural killer (**NK**) cell-mediated lysis by interacting with CD94/**NKG2A** receptors. Surface expression of **HLA-E** depends on binding of conserved peptides derived from MHC class I mols. The same peptide is present in the leader sequence of the human cytomegalovirus (HCMV) glycoprotein UL40 (gpUL40). It is shown that, independently of the transporter assocd. with antigen processing, gpUL40 can up-regulate expression of **HLA-E**, which protects targets from **NK** cell lysis. While classical MHC class I mols. are down-regulated, **HLA-E** is up-regulated by HCMV. Induction of **HLA-E** surface expression by gpUL40 may represent an escape route for HCMV.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Surface expression of **HLA-E**, an inhibitor of natural killer cells, enhanced by human cytomegalovirus gpUL40

AU Tomasec, Peter; **Braud, Veronique M.**; Rickards, Carole; Powell, Martin B.; McSharry, Brian P.; Gadola, Stephan; Cerundolo, Vincenzo; Borysiewicz, Leszek K.; **McMichael, Andrew J.**; Wilkinson, Gavin W. G.

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IT Antigen receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(CD94/**NKG2A**; human cytomegalovirus gpUL40 upregulates surface expression of **HLA-E**, protects against lysis by CD94/**NKG2A** natural killer cells, and contains the same peptide as **HLA-E** derived from MHC class I mols.)

IT CD antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(CD94; human cytomegalovirus gpUL40 upregulates surface expression of **HLA-E**, protects against lysis by CD94/**NKG2A** natural killer cells, and contains the same peptide as **HLA-E** derived from MHC class I mols.)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**HLA-E**; human cytomegalovirus gpUL40 upregulates

surface expression of **HLA-E**, protects against lysis by CD94/**NKG2A** natural killer cells, and contains the same peptide as **HLA-E** derived from MHC class I mols.)

IT Glycoproteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(UL40; human cytomegalovirus gpUL40 upregulates surface expression of **HLA-E**, protects against lysis by CD94/**NKG2A** natural killer cells, and contains the same peptide as **HLA-E** derived from MHC class I mols.)

IT Cytotoxicity
Human herpesvirus 5
(human cytomegalovirus gpUL40 upregulates surface expression of **HLA-E**, protects against lysis by CD94/**NKG2A** natural killer cells, and contains the same peptide as **HLA-E** derived from MHC class I mols.)

IT Signal peptides
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(human cytomegalovirus gpUL40 upregulates surface expression of **HLA-E**, protects against lysis by CD94/**NKG2A** natural killer cells, and contains the same peptide as **HLA-E** derived from MHC class I mols.)

IT Lymphocyte
(natural killer cell; human cytomegalovirus gpUL40 upregulates surface expression of **HLA-E**, protects against lysis by CD94/**NKG2A** natural killer cells, and contains the same peptide as **HLA-E** derived from MHC class I mols.)

IT Infection
(viral; human cytomegalovirus gpUL40 upregulates surface expression of **HLA-E**, protects against lysis by CD94/**NKG2A** natural killer cells, and contains the same peptide as **HLA-E** derived from MHC class I mols.)

IT 264585-39-9 264585-40-2 264585-41-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; human cytomegalovirus gpUL40 upregulates surface expression of **HLA-E**, protects against lysis by CD94/**NKG2A** natural killer cells, and contains the same peptide as **HLA-E** derived from MHC class I mols.)

IT 205491-11-8
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(human cytomegalovirus gpUL40 upregulates surface expression of **HLA-E**, protects against lysis by CD94/**NKG2A** natural killer cells, and contains the same peptide as **HLA-E** derived from MHC class I mols.)

L4 ANSWER 6 OF 14 MEDLINE
ACCESSION NUMBER: 2000134720 MEDLINE
DOCUMENT NUMBER: 20134720 PubMed ID: 10669413
TITLE: Surface expression of **HLA-E**, an inhibitor of natural killer cells, enhanced by human cytomegalovirus gpUL40.
AUTHOR: Tomasec P; **Braud V M**; Rickards C; Powell M B; McSharry B P; Gadola S; Cerundolo V; Borysiewicz L K; **McMichael A J**; Wilkinson G W
CORPORATE SOURCE: Department of Medicine, University of Wales College of Medicine, Cardiff CF14 4XN, UK.
SOURCE: SCIENCE, (2000 Feb 11) 287 (5455) 1031.
Journal code: 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000309
Last Updated on STN: 20000309
Entered Medline: 20000224

AB The nonclassical major histocompatibility complex (MHC) class I molecule **HLA-E** inhibits natural killer (**NK**) cell-mediated lysis by interacting with CD94/**NKG2A** receptors. Surface expression of **HLA-E** depends on binding of conserved peptides derived from MHC class I molecules. The same peptide is present in the leader sequence of the human cytomegalovirus (HCMV) glycoprotein UL40 (gpUL40). It is shown that, independently of the transporter associated with antigen processing, gpUL40 can up-regulate expression of **HLA-E**, which protects targets from **NK** cell lysis. While classical MHC class I molecules are down-regulated, **HLA-E** is up-regulated by HCMV. Induction of **HLA-E** surface expression by gpUL40 may represent an escape route for HCMV.

TI Surface expression of **HLA-E**, an inhibitor of natural killer cells, enhanced by human cytomegalovirus gpUL40.

AU Tomasec P; **Braud V M**; Rickards C; Powell M B; McSharry B P; Gadola S; Cerundolo V; Borysiewicz L K; **McMichael A J**; Wilkinson G W

AB The nonclassical major histocompatibility complex (MHC) class I molecule **HLA-E** inhibits natural killer (**NK**) cell-mediated lysis by interacting with CD94/**NKG2A** receptors. Surface expression of **HLA-E** depends on binding of conserved peptides derived from MHC class I molecules. The same peptide is present in the leader. . . glycoprotein UL40 (gpUL40). It is shown that, independently of the transporter associated with antigen processing, gpUL40 can up-regulate expression of **HLA-E**, which protects targets from **NK** cell lysis. While classical MHC class I molecules are down-regulated, **HLA-E** is up-regulated by HCMV. Induction of **HLA-E** surface expression by gpUL40 may represent an escape route for HCMV.

CN 0 (HLA Antigens); 0 (**HLA-E** antigen); 0 (Histocompatibility Antigens Class I); 0 (Protein Sorting Signals); 0 (Receptors, Immunologic); 0 (Recombinant Fusion Proteins); 0 (UL40 glycoprotein,. . .

L4 ANSWER 7 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:479385 BIOSIS
DOCUMENT NUMBER: PREV200000479385
TITLE: **HLA-E** is expressed on trophoblast and interacts with CD94/**NKG2** receptors on decidual **NK** cells.
AUTHOR(S): King, A. (1); **Allan, D. S. J. (1)**; Bowen, J. M. (1); Powis, S. J. (1); Joseph, S. (1); Verma, S. (1); Hiby,

S. E. (1); **McMichael, A. J.** (1); Loke, Y. W. (1); **Braud, V. M.** (1)

CORPORATE SOURCE: (1) Department of Pathology, University of Cambridge, Cambridge UK

SOURCE: Placenta, (September, 2000) Vol. 21, No. 7, pp. A.39. print.
Meeting Info.: 14th Rochester Trophoblast Conference Meeting in Association with the Society for the Investigation of Early Pregnancy and the 6th Meeting of the International Federation of Placental Associations Rochester, New York, USA October 04-08, 2000
ISSN: 0143-4004.

DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

TI **HLA-E** is expressed on trophoblast and interacts with CD94/**NKG2** receptors on decidual **NK** cells.

AU King, A. (1); **Allan, D. S. J.** (1); Bowen, J. M. (1); Powis, S. J. (1); Joseph, S. (1); Verma, S. (1); Hiby, S. E. (1); **McMichael, A. J.** (1); Loke, Y. W. (1); **Braud, V. M.** (1)

IT Major Concepts
Immune System (Chemical Coordination and Homeostasis); Reproductive System (Reproduction)

IT Chemicals & Biochemicals
CD-94-**NKG**-2 receptor: **HLA-e** histocompatibility antigen interaction, decidual natural killer cell expression; **HLA-E** histocompatibility antigen: trophoblast expression

L4 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:375752 CAPLUS
DOCUMENT NUMBER: 131:18007

TITLE: **HLA-E** binding

INVENTOR(S): **Braud, Veronique M.**; **Allan, David S. J.**; **Ogg, Graham S.**; O'Callaghan, Christopher A.; **McMichael, Andrew J.**

PATENT ASSIGNEE(S): Isis Innovation Limited, UK

SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9928748	A2	19990610	WO 1998-GB3686	19981204
WO 9928748	A3	19991223		
W: JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1036327	A2	20000920	EP 1998-959027	19981204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, PI				
JP 2002513541	T2	20020514	JP 2000-523554	19981204

PRIORITY APPLN. INFO.: GB 1997-25764 A 19971204
WO 1998-GB3686 W 19981204

AB The invention relates to a method of causing an interaction of CD94/**NKG2**+ cells, which method comprises contacting the cells with recombinant **HLA-E** under binding conditions. The **HLA-E** property of binding to CD94/**NKG2** receptors on **NK** cells and a subset of CD8+ T cells is useful for targeting CD94/**NKG2**+ cells for a variety of purposes such as identification, isolation, killing or inactivation. In another word, the invention is useful for diagnostic and therapeutic purposes in a variety of conditions including cancer, lymphomas and leukemias, infections, prevention of fetus rejection, transplant rejection or graft-vs-host disease, immunodeficiency, and other autoimmune diseases (systemic lupus erythematosus, diabetes, thyroid diseases, vitiligo, rheumatoid arthritis, etc.). Thus, tetrameric complexes comprising biotinylated **HLA-E**, .beta.2m, signal sequence of HLA-B*0801, and phycoerythrin-labeled extravidin were prepd. and tested for binding to **NK** cells and a subset of T cells. **HLA-E** -coated beads were prepd. for isolating CD94/**NKG2**+ cells, and recombinant biotinylated **HLA-E** coupled to perforin-linked extravidin was described for killing **NK** cells. Recombinant **HLA-E** with **HLA**-B8 leader sequence was generated for use in xenotransplantation.

TI **HLA-E** binding

IN **Braud, Veronique M.**; **Allan, David S. J.**; **Ogg, Graham S.**; O'Callaghan, Christopher A.; **McMichael, Andrew J.**

AB The invention relates to a method of causing an interaction of CD94/**NKG2**+ cells, which method comprises contacting the cells with recombinant **HLA-E** under binding conditions. The **HLA-E** property of binding to CD94/**NKG2** receptors on **NK** cells and a subset of CD8+ T cells is useful for targeting CD94/**NKG2**+ cells for a variety of purposes such as identification, isolation, killing or inactivation. In another word, the invention is useful for diagnostic and therapeutic purposes in a variety of conditions including cancer, lymphomas and leukemias, infections, prevention of fetus rejection, transplant rejection or graft-vs-host disease, immunodeficiency, and other autoimmune diseases (systemic lupus erythematosus, diabetes, thyroid diseases, vitiligo, rheumatoid arthritis, etc.). Thus, tetrameric complexes comprising biotinylated **HLA-E**, .beta.2m, signal sequence of HLA-B*0801, and phycoerythrin-labeled extravidin were prepd. and tested for binding to **NK** cells and a subset of T cells. **HLA-E** -coated beads were prepd. for isolating CD94/**NKG2**+ cells, and recombinant biotinylated **HLA-E** coupled to perforin-linked extravidin was described for killing **NK** cells. Recombinant **HLA-E** with **HLA**-B8 leader sequence was generated for use in xenotransplantation.

ST **HLA E** CD94NKG2 **NK** T cell

IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(CD94/**NKG2**; **HLA-E** binding for detecting, isolating, killing or inactivating CD94/**NKG2**+ **NK** cells and T cells and for diagnostic/therapeutic purposes in cancer, infection, transplantation or autoimmune disease)

IT T cell (lymphocyte)
(CD94/**NKG2**+; **HLA-E** binding for detecting,

isolating, killing or inactivating CD94/NKG2+ NK cells and T cells and for diagnostic/therapeutic purposes in cancer, infection, transplantation or autoimmune disease)

IT CD antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(CD94; HLA-E binding for detecting, isolating, killing or inactivating CD94/NKG2+ NK cells and T cells and for diagnostic/therapeutic purposes in cancer, infection, transplantation or autoimmune disease)

IT Autoimmune disease
Diabetes mellitus
Immunodeficiency
Infection
Leukemia
Lymphoma
Neoplasm
Rheumatoid arthritis
Thyroid gland, disease
Transplant rejection
Vitiligo
(HLA-E binding for detecting, isolating, killing or inactivating CD94/NKG2+ NK cells and T cells and for diagnostic/therapeutic purposes in cancer, infection, transplantation or autoimmune disease)

IT Gene, animal
Nucleic acids
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HLA-E binding for detecting, isolating, killing or inactivating CD94/NKG2+ NK cells and T cells and for diagnostic/therapeutic purposes in cancer, infection, transplantation or autoimmune disease)

IT Avidins
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HLA-E binding for detecting, isolating, killing or inactivating CD94/NKG2+ NK cells and T cells and for diagnostic/therapeutic purposes in cancer, infection, transplantation or autoimmune disease)

IT Histocompatibility antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HLA-E; HLA-E binding for detecting, isolating, killing or inactivating CD94/NKG2+ NK cells and T cells and for diagnostic/therapeutic purposes in cancer, infection, transplantation or autoimmune disease)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(MHC (major histocompatibility complex), class I, receptors, NKG2; HLA-E binding for detecting, isolating, killing or inactivating CD94/NKG2+ NK cells and T cells and for diagnostic/therapeutic purposes in cancer, infection, transplantation or autoimmune disease)

IT Mammal (Mammalia)
(cells; HLA-E binding for detecting, isolating, killing or inactivating CD94/NKG2+ NK cells and T cells and for diagnostic/therapeutic purposes in cancer, infection, transplantation or autoimmune disease)

IT Chemistry
(chem. compds., testing; HLA-E binding for detecting, isolating, killing or inactivating CD94/NKG2+ NK cells and T cells and for diagnostic/therapeutic purposes in cancer, infection, transplantation or autoimmune disease)

IT Toxins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(delivery; HLA-E binding for detecting, isolating, killing or inactivating CD94/NKG2+ NK cells and T cells and for diagnostic/therapeutic purposes in cancer, infection, transplantation or autoimmune disease)

IT Avidins
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(extr-; HLA-E binding for detecting, isolating, killing or inactivating CD94/NKG2+ NK cells and T cells and for diagnostic/therapeutic purposes in cancer, infection, transplantation or autoimmune disease)

IT Pregnancy
(fetus rejection prevention; HLA-E binding for detecting, isolating, killing or inactivating CD94/NKG2+ NK cells and T cells and for diagnostic/therapeutic purposes in cancer, infection, transplantation or autoimmune disease)

IT Embryo, animal
(fetus, rejection prevention; HLA-E binding for detecting, isolating, killing or inactivating CD94/NKG2+ NK cells and T cells and for diagnostic/therapeutic purposes in cancer, infection, transplantation or autoimmune disease)

IT Transplant and Transplantation
(graft-vs.-host reaction; HLA-E binding for detecting, isolating, killing or inactivating CD94/NKG2+ NK cells and T cells and for diagnostic/therapeutic purposes in cancer, infection, transplantation or autoimmune disease)

IT Lymphocyte
(natural killer cell, CD94/NKG2+; HLA-E binding for detecting, isolating, killing or inactivating CD94/NKG2+ NK cells and T cells and for diagnostic/therapeutic purposes in cancer, infection, transplantation or autoimmune disease)

IT Lupus erythematosus
(systemic; HLA-E binding for detecting, isolating, killing or inactivating CD94/NKG2+ NK cells and T cells and for diagnostic/therapeutic purposes in cancer, infection, transplantation or autoimmune disease)

IT Animal tissue
Organ, animal
(xenogeneic; HLA-E binding for detecting, isolating, killing or inactivating CD94/NKG2+ NK cells and T cells and for diagnostic/therapeutic purposes in cancer, infection, transplantation or autoimmune disease)

IT 9013-20-1, Streptavidin
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**HLA-E** binding for detecting, isolating, killing or inactivating CD94/**NKG2+** **NK** cells and T cells and for diagnostic/therapeutic purposes in cancer, infection, transplantation or autoimmune disease)

IT 58-85-5, Biotin
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**HLA-E** binding for detecting, isolating, killing or inactivating CD94/**NKG2+** **NK** cells and T cells and for diagnostic/therapeutic purposes in cancer, infection, transplantation or autoimmune disease)

L4 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:100537 CAPLUS
DOCUMENT NUMBER: 130:266111
TITLE: MHC class I triggering by a novel cell surface ligand costimulates proliferation of activated human T cells
AUTHOR(S): Agrawal, Samir; Marquet, Jeanine; Freeman, Gordon J.; Tawab, Abdul; Le Bouteiller, Philippe; Roth, Patricia; Bolton, Wade; **Ogg, Graham**; Boumsell, Laurence; Bensussan, Armand
CORPORATE SOURCE: Institut National de la Sante et de la Recherche Medicale U448, Faculte de Medecine, Henri Mondor Hospital, Creteil, Fr.
SOURCE: Journal of Immunology (1999), 162(3), 1223-1226
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB BY55 is a human cell surface mol. whose expression is restricted to **NK** cells, a subset of circulating CD8+ T lymphocytes, and all intestinal intraepithelial T lymphocytes. Here, the authors report that BY55 is a novel **NK** receptor showing broad specificity for both classical and nonclassical MHC class I mols., and that optimal binding requires a prior aggregation of MHC class I complexes. Using BY55 transfectants, the authors have identified functional consequences of MHC class I/ligand interactions for the class I-bearing cell. The triggering of MHC class I mols. on human T cell clones by BY55 delivered a potent proliferative signal in the presence of sol. CD3 mAb. The costimulatory signal provided by MHC class I ligation was only seen in activated, and not resting, peripheral blood T cells. This observation represents an addnl. and/or alternative pathway to CD28 costimulation and may be of particular relevance in memory T cells lacking CD28, such as intestinal intraepithelial T lymphocytes, which are CD28- but BY55+.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
AU Agrawal, Samir; Marquet, Jeanine; Freeman, Gordon J.; Tawab, Abdul; Le Bouteiller, Philippe; Roth, Patricia; Bolton, Wade; **Ogg, Graham**; Boumsell, Laurence; Bensussan, Armand
AB BY55 is a human cell surface mol. whose expression is restricted to **NK** cells, a subset of circulating CD8+ T lymphocytes, and all intestinal intraepithelial T lymphocytes. Here, the authors report that BY55 is a novel **NK** receptor showing broad specificity for both classical and nonclassical MHC class I mols., and that optimal binding requires a prior aggregation of MHC class I complexes. Using BY55 transfectants, the authors have identified functional consequences of MHC class I/ligand interactions for the class I-bearing cell. The triggering of MHC class I mols. on human T cell clones by BY55 delivered a potent proliferative signal in the presence of sol. CD3 mAb. The costimulatory signal provided by MHC class I ligation was only seen in activated, and not resting, peripheral blood T cells. This observation represents an addnl. and/or alternative pathway to CD28 costimulation and may be of particular relevance in memory T cells lacking CD28, such as intestinal intraepithelial T lymphocytes, which are CD28- but BY55+.
IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**HLA-E**; BY55 as ligand for)

L4 ANSWER 10 OF 14 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 1999158668 MEDLINE
DOCUMENT NUMBER: 99158668 PubMed ID: 10047540
TITLE: Functions of nonclassical MHC and non-MHC-encoded class I molecules.
AUTHOR: **Braud V M**; **Allan D S**; **McMichael A J**
CORPORATE SOURCE: Institute of Molecular Medicine, John Radcliffe Hospital, Oxford, UK.. vbraud@worf.molbiol.ox.ac.uk
SOURCE: CURRENT OPINION IN IMMUNOLOGY, (1999 Feb) 11 (1) 100-8. Ref: 85
Journal code: 8900118. ISSN: 0952-7915.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990326
Last Updated on STN: 19990326
Entered Medline: 19990317
AB Fascinating recent discoveries have focused attention on the nonclassical class I molecules. They can exert their function at most levels of the immune response, being part of both innate and adaptive immune systems. They not only have specialized antigen-presentation functions but also play important immunoregulatory roles: **HLA-E** regulates natural killer cells by interacting with CD94/**NKG2** receptors; the MIC (MHC class I chain related) glycoproteins appear crucial to the activation of gammadelta T cells in the gastrointestinal epithelium; HLA-G may play a role in controlling the immune response to the fetus; and CD1 molecules are important in defense against bacterial infections, as well as in the development and regulation of a subset of **NKT** cells expressing a highly restricted TCR repertoire; however not all nonclassical class I molecules have an immunological function, as demonstrated by HFE which is implicated in iron metabolism.
AU **Braud V M**; **Allan D S**; **McMichael A J**
AB . . . of both innate and adaptive immune systems. They not only have specialized antigen-presentation functions but also play important immunoregulatory roles: **HLA-E** regulates natural killer

cells by interacting with CD94/**NKG2** receptors; the MIC (MHC class I chain related) glycoproteins appear crucial to the activation of gammadelta T cells in the. . . molecules are important in defense against bacterial infections, as well as in the development and regulation of a subset of **NKT** cells expressing a highly restricted TCR repertoire; however not all nonclassical class I molecules have an immunological function, as demonstrated. . .

CN 0 (Antigens, CD1); 0 (HLA Antigens); 0 (**HLA-E** antigen); 0 (HLA-G antigen); 0 (HLA-H antigen); 0 (Histocompatibility Antigens Class I); 0 (MICA protein); 0 (MICB antigen); 0 (Q. . .

L4 ANSWER 11 OF 14 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 1999383027 MEDLINE
DOCUMENT NUMBER: 99383027 PubMed ID: 10453651
TITLE: Regulation of **NK** cell functions through interaction of the CD94/**NKG2** receptors with the nonclassical class I molecule **HLA-E**.
AUTHOR: **Braud V M**; **McMichael A J**
CORPORATE SOURCE: Institute of Molecular Medicine, Headington, Oxford, UK.
SOURCE: CURRENT TOPICS IN MICROBIOLOGY AND IMMUNOLOGY, (1999) 244 85-95. Ref: 30
Journal code: 0110513. ISSN: 0070-217X.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 19991014
Last Updated on STN: 19991014
Entered Medline: 19991006

TI Regulation of **NK** cell functions through interaction of the CD94/**NKG2** receptors with the nonclassical class I molecule **HLA-E**.

AU **Braud V M**; **McMichael A J**

CN 0 (Antigens, CD); 0 (HLA Antigens); 0 (**HLA-E** antigen); 0 (Histocompatibility Antigens Class I); 0 (Ligands); 0 (Membrane Glycoproteins); 0 (**NKG2** protein); 0 (Peptides); 0 (Receptors, Immunologic); 0 (antigen CD94)

L4 ANSWER 12 OF 14 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 1998146055 MEDLINE
DOCUMENT NUMBER: 98146055 PubMed ID: 9486650
TITLE: **HLA-E** binds to natural killer cell receptors CD94/**NKG2A**, B and C.
COMMENT: Comment in: Nature. 1998 Feb 19;391(6669):740-1, 743
AUTHOR: **Braud V M**; **Allan D S**; O'Callaghan C A; Soderstrom K; D'Andrea A; **Ogg G S**; Lazetic S; Young N T; Bell J I; Phillips J H; Lanier L L; **McMichael A J**
CORPORATE SOURCE: Institute of Molecular Medicine, John Radcliffe Hospital, Oxford, UK.. vbraud@worf.molbiol.ox.ac.uk
SOURCE: NATURE, (1998 Feb 19) 391 (6669) 795-9.
Journal code: 0410462. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199803
ENTRY DATE: Entered STN: 19980319
Last Updated on STN: 19980319
Entered Medline: 19980309

AB The protein **HLA-E** is a non-classical major histocompatibility complex (MHC) molecule of limited sequence variability. Its expression on the cell surface is regulated by the binding of peptides derived from the signal sequence of some other MHC class I molecules. Here we report the identification of ligands for **HLA-E**. We constructed tetramers in which recombinant **HLA-E** and beta2-microglobulin were refolded with an MHC leader-sequence peptide, biotinylated, and conjugated to phycoerythrin-labelled Extravidin. This **HLA-E** tetramer bound to natural killer (**NK**) cells and a small subset of T cells from peripheral blood. On transfectants, the tetramer bound to the CD94/**NKG2A**, CD94/**NKGK2B** and CD94/**NKG2C** **NK** cell receptors, but did not bind to the immunoglobulin family of **NK** cell receptors (KIR). Surface expression of **HLA-E** was enough to protect target cells from lysis by CD94/**NKG2A**+ **NK**-cell clones. A subset of HLA class I alleles has been shown to inhibit killing by CD94/**NKG2A**+ **NK**-cell clones. Only the HLA alleles that possess a leader peptide capable of upregulating **HLA-E** surface expression confer resistance to **NK**-cell-mediated lysis, implying that their action is mediated by **HLA-E**, the predominant ligand for the **NK** cell inhibitory receptor CD94/**NKG2A**.

TI **HLA-E** binds to natural killer cell receptors CD94/**NKG2A**, B and C.

AU **Braud V M**; **Allan D S**; O'Callaghan C A; Soderstrom K; D'Andrea A; **Ogg G S**; Lazetic S; Young N T; Bell J I; Phillips J H; Lanier L L; **McMichael A J**

AB The protein **HLA-E** is a non-classical major histocompatibility complex (MHC) molecule of limited sequence variability. Its expression on the cell surface is regulated. . . derived from the signal sequence of some other MHC class I molecules. Here we report the identification of ligands for **HLA-E**. We constructed tetramers in which recombinant **HLA-E** and beta2-microglobulin were refolded with an MHC leader-sequence peptide, biotinylated, and conjugated to phycoerythrin-labelled Extravidin. This **HLA-E** tetramer bound to natural killer (**NK**) cells and a small subset of T cells from peripheral blood. On transfectants, the tetramer bound to the CD94/**NKG2A**, CD94/**NKGK2B** and CD94/**NKG2C** **NK** cell receptors, but did not bind to the immunoglobulin family of **NK** cell receptors (KIR). Surface expression of **HLA-E** was enough to protect target cells from lysis by CD94/**NKG2A**+ **NK**-cell clones. A subset of HLA class I alleles has been shown to inhibit killing by CD94/**NKG2A**+ **NK**-cell clones. Only the HLA alleles that possess a leader peptide capable of upregulating **HLA-E** surface expression confer resistance to **NK**-cell-mediated lysis, implying that their action is mediated by **HLA-E**, the predominant ligand for the **NK** cell inhibitory receptor CD94/**NKG2A**.

CN 0 (Antigens, CD); 0 (HLA Antigens); 0 (**HLA-E** antigen); 0 (Histocompatibility Antigens Class I); 0 (Ligands); 0 (Membrane Glycoproteins); 0 (**NKG2** protein); 0 (Protein Sorting Signals); 0 (Receptors, Immunologic); 0 (Recombinant Proteins); 0 (antigen CD94); 0 (beta 2-Microglobulin); 0 (killer inhibitory. . .

L4 ANSWER 13 OF 14 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 1998325367 MEDLINE
DOCUMENT NUMBER: 98325367 PubMed ID: 9660937
TITLE: Structural features impose tight peptide binding specificity in the nonclassical MHC molecule **HLA-E**.
AUTHOR: O'Callaghan C A; Tormo J; Willcox B E; **Braud V M**; Jakobsen B K; Stuart D I; **McMichael A J**; Bell J I; Jones E Y
CORPORATE SOURCE: Nuffield Department of Clinical Medicine, University of Oxford, John Radcliffe Hospital, United Kingdom.
SOURCE: MOLECULAR CELL, (1998 Mar) 1 (4) 531-41.
Journal code: 9802571. ISSN: 1097-2765.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199807
ENTRY DATE: Entered STN: 19980811
Last Updated on STN: 19980811
Entered Medline: 19980728

AB The crystal structure of the nonclassical human class 1b MHC molecule **HLA-E** has been determined in complex with a prototypic ligand, the nonamer peptide (VMAPRTVLL), derived from the highly conserved residues 3-11 of the human MHC class 1a leader sequence. The mode of peptide binding retains some of the standard features observed in MHC class 1a complexes, but novel features imply that **HLA-E** has evolved to mediate specific binding to a tightly defined set of almost identical hydrophobic peptides from the highly conserved class 1 leader sequences. These molecular adaptations make **HLA-E** a rigorous checkpoint at the cell surface reporting on the integrity of the antigen processing pathway to CD94/**NKG2** receptor-bearing natural killer cells.

TI Structural features impose tight peptide binding specificity in the nonclassical MHC molecule **HLA-E**.

AU O'Callaghan C A; Tormo J; Willcox B E; **Braud V M**; Jakobsen B K; Stuart D I; **McMichael A J**; Bell J I; Jones E Y

AB The crystal structure of the nonclassical human class 1b MHC molecule **HLA-E** has been determined in complex with a prototypic ligand, the nonamer peptide (VMAPRTVLL), derived from the highly conserved residues 3-11. . . of peptide binding retains some of the standard features observed in MHC class 1a complexes, but novel features imply that **HLA-E** has evolved to mediate specific binding to a tightly defined set of almost identical hydrophobic peptides from the highly conserved class 1 leader sequences. These molecular adaptations make **HLA-E** a rigorous checkpoint at the cell surface reporting on the integrity of the antigen processing pathway to CD94/**NKG2** receptor-bearing natural killer cells.

CN 0 (HLA Antigens); 0 (HLA-B8 Antigen); 0 (**HLA-E** antigen); 0 (Histocompatibility Antigens Class I); 0 (Peptide Fragments)

L4 ANSWER 14 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:219821 BIOSIS
DOCUMENT NUMBER: PREV199900219821
TITLE: Decidual **NK** cells have receptors for **HLA**-**E** which is expressed by human trophoblast.
AUTHOR(S): **Allan, D.S.J.** (1); Verma, S.; Bowen, J. M.; Loke, Y. W.; McMichael, J. (1); **Braud, V. M.** (1); King, A.
CORPORATE SOURCE: (1) Institute of Molecular Medicine, John Radcliffe Hospital, Oxford, OX3 9DS UK
SOURCE: Natural Immunity, (Feb., 1998) Vol. 16, No. 2-3, pp. 79.
Meeting Info.: Fifth Annual Meeting of the Society for Natural Immunity Seventeenth International Natural Killer Cell Workshop Warrenton, Virginia, USA October 17-21, 1998
ISSN: 1018-8916.
DOCUMENT TYPE: Conference
LANGUAGE: English

TI Decidual **NK** cells have receptors for **HLA-E** which is expressed by human trophoblast.

AU **Allan, D.S.J.** (1); Verma, S.; Bowen, J. M.; Loke, Y. W.; McMichael, J. (1); **Braud, V. M.** (1); King, A.

IT . . .
Homeostasis)

IT Parts, Structures, & Systems of Organisms
natural killer cells: blood and lymphatics, immune system

IT Chemicals & Biochemicals
HLA-E receptor; **HLA-E**: expression

```
=> duis his
DUIS IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> dis his

     (FILE 'HOME' ENTERED AT 13:53:22 ON 24 JUN 2002)

     FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 13:53:34 ON 24 JUN 2002
L1          3511 S BRAUD V?/AU OR ALLAN D?/AU OR OGG G?/AU OR OCALLAGHAN C?/AU O
L2            47 S L1 AND (NK?)
L3            35 S L2 AND (HLA (1N) E)
L4            14 DUP REM L3 (21 DUPLICATES REMOVED)

=> s nk (P) (NK? or CD94?)
L5         72958 NK (P) (NK? OR CD94?)

=> s (HLA (1N) E) (P) (NK? or CD94?)
L6           315 (HLA (1N) E) (P) (NK? OR CD94?)

=> s l6 and PD<19981204
'19981204' NOT A VALID FIELD CODE
   3 FILES SEARCHED...
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L8 ANSWER 1 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
TI **HLA-E** is a major ligand for the natural killer inhibitory receptor **CD94/NKG2A**
SO Proceedings of the National Academy of Sciences of the United States of America (**1998**), 95(9), 5199-5204
CODEN: PNASA6; ISSN: 0027-8424
AB . . . a nonamer peptide derived from certain HLA class I signal sequences is a necessary requirement for the stabilization of endogenous **HLA-E** expression on the surface of 721.221 cells. This led the authors to examine the ability of **HLA-E** to protect HLA class I transfectants from natural killer (**NK**) cell-mediated lysis. It was possible to implicate the **CD94/NKG2A** complex as an inhibitory receptor recognizing this class Ib mol. by using as target a .221 transfectant selectively expressing surface **HLA-E**. **HLA-E** had no apparent inhibitory effect mediated through the identified Ig superfamily (Ig-SF) human killer cell inhibitory receptors or ILT2/LIR1. Further studies of **CD94/NKG2+ NK** cell-mediated recognition of .221 cells transfected with different HLA class I allotypes (i.e., -Cw4, -Cw3, -B7) confirmed that the inhibitory interaction was mediated by **CD94/NKG2A** recognizing the surface **HLA-E** mol., because only antibodies directed against either **HLA-E**, **CD94**, or **CD94/NKG2A** specifically restored lysis. Surface stabilization of **HLA-E** in cold-treated .221 cells loaded with appropriate peptides was sufficient to confer protection, resulting from recognition of the HLA class Ib mol. by the **CD94/NKG2A** inhibitory receptor. Consistent with the prediction that the ligand for **CD94/NKG2A** is expressed ubiquitously, the authors' examn. of **HLA-E** antigen distribution indicated that it is detectable on the surface of a wide variety of cell types.
ST **HLA E** ligand natural killer receptor; **CD94** **NKG2A** receptor **HLA E** ligand
IT CD antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**CD94**, complexes with **NKG2A**; **HLA-E** is ligand for natural killer inhibitory receptor **CD94/NKG2A**)
IT Ligands
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**HLA-E** is ligand for natural killer inhibitory receptor **CD94/NKG2A**)
IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**HLA-E**; **HLA-E** is ligand for natural killer inhibitory receptor **CD94/NKG2A**)
IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**NKG2A**, complexes with **CD94**; **HLA-E** is ligand for natural killer inhibitory receptor **CD94/NKG2A**)
IT Cytolysis
(natural killer cell-mediated; **HLA-E** is ligand for natural killer inhibitory receptor **CD94/NKG2A**)
IT Lymphocyte
(natural killer cell; **HLA-E** is ligand for natural killer inhibitory receptor **CD94/NKG2A**)

L8 ANSWER 2 OF 30 CAPLUS COPYRIGHT 2002 ACS
SO Proceedings of the National Academy of Sciences of the United States of America (**1998**), 95(9), 4791-4794
CODEN: PNASA6; ISSN: 0027-8424
AB A review and discussion with 44 refs. There are abundant data to substantiate the conclusion that **CD94/NKG2A** receptors of human natural killer cells directly recognize **HLA-E** mols.
IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**HLA-E**; **HLA** class I specificity for natural killer cell receptor **CD94/NKG2A**)

L8 ANSWER 3 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
SO European Journal of Immunology (**1998**), 28(12), 4356-4361
CODEN: EJIMAF; ISSN: 0014-2980
AB Recent studies on human **NK** cells have demonstrated that the **NK** cell **CD94/NKG2** receptors bind to the nonclassical MHC class I mol. **HLA-E**. A functional **CD94/NKG2** complex has not yet been identified in rodents, but cDNA encoding rat and mouse **CD94** and **NKG2** have recently been cloned, suggesting that **CD94/NKG2** receptors may exist in species other than man. The mouse nonclassical MHC class I mol. Qa-1 shares several features with **HLA-E**. This suggests that Qa-1 may be similarly recognized by murine **NK** cells. To study the ability of Qa-1 to bind to murine **NK** cells, the authors have produced a sol. tetrameric form of Qa-1b. The authors demonstrate that Qa-1b tetramers distinctly bind to a large subset of fresh or IL-2-activated **NK1.1+**/CD3- splenocytes independently of the expression of Ly49 inhibitory receptors. Binding occurs whether **NK** cells have evolved in an MHC class I-expressing or in an MHC class I-deficient environment. The data suggest the existence of a Qa-1-recognizing structure on a large subpopulation of murine **NK** cells that may be similar to the human **CD94/NKG2** heterodimeric complex.

L8 ANSWER 4 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
TI **HLA-E**-bound peptides influence recognition by inhibitory and triggering **CD94/NKG2** receptors. Preferential response to an HLA-G-derived nonamer
SO European Journal of Immunology (**1998**), 28(9), 2854-2863

CODEN: EJIMAF; ISSN: 0014-2980

AB The **HLA-E** class Ib mol. constitutes a major ligand for the lectin-like **CD94/NKG2** natural killer (**NK**) cell receptors. Specific HLA class I leader sequence-derived nonapeptides bind to endogenous **HLA-E** mols. in the HLA-defective cell line 721.221, inducing **HLA-E** surface expression, and promote **CD94/NKG2A**-mediated recognition. The authors compared the ability of **NK** clones which expressed either inhibitory or activating **CD94/NKG2** receptors to recognize **HLA-E** mols. on the surface of 721.221 cells loaded with a panel of synthetic nonamers derived from the leader sequences of most HLA class I mols. The results support the notion that the primary structure of the **HLA-E**-bound peptides influences **CD94/NKG2**-mediated recognition, beyond their ability to stabilize surface **HLA-E**. **CD94/NKG2A+ NK** clones appeared more sensitive to the interaction with most **HLA-E**-peptide complexes than did effector cells expressing the activating **CD94/NKG2C** receptor. An exception to this pattern was I-ILA-E loaded with the HLA-G-derived nonamer. This complex triggered cytotoxicity very efficiently over a wide range of peptide concns., suggesting that the **HLA-E**/G-nonamer complex interacts with the **CD94/NKG2** triggering receptor with a higher affinity. These results raise the possibility that **CD94/NKG2**-mediated recognition of **HLA-E** expressed on extravillous cytotrophoblasts plays an important role in maternal-fetal cellular interactions.

IT CD antigens
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**CD94**; **HLA-E**-bound peptides influence recognition by inhibitory and triggering **CD94/NKG2** receptors)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**HLA-E** antigen; **HLA-E**-bound peptides influence recognition by inhibitory and triggering **CD94/NKG2** receptors)

IT Histocompatibility antigens
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**HLA-E**, Ib, complex wit peptides; **HLA-E**-bound peptides influence recognition by inhibitory and triggering **CD94/NKG2** receptors)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**HLA-E**, receptors; **HLA-E**-bound peptides influence recognition by inhibitory and triggering **CD94/NKG2** receptors)

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HLA-G; **HLA-E**-bound peptides influence recognition by inhibitory and triggering **CD94/NKG2** receptors)

IT Receptors
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**NKG2**; **HLA-E**-bound peptides influence recognition by inhibitory and triggering **CD94/NKG2** receptors)

IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(complex with **HLA-E** class Ib; **HLA-E**-bound peptides influence recognition by inhibitory and triggering **CD94/NKG2** receptors)

IT Trophoblast
(cytotrophoblast; **HLA-E**-bound peptides influence recognition by inhibitory and triggering **CD94/NKG2** receptors in relation to)

IT Lymphocyte
(natural killer cell; **HLA-E**-bound peptides influence recognition by inhibitory and triggering **CD94/NKG2** receptors)

IT 193002-77-6 202657-59-8 202657-60-1 202657-61-2 202657-62-3
205491-11-8 214621-61-1 215439-93-3 215439-97-7 215440-00-9
215440-04-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**HLA-E**-bound peptides influence recognition by inhibitory and triggering **CD94/NKG2** receptors)

L8 ANSWER 5 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 4

TI Specific engagement of the **CD94/NKG2**-A killer inhibitory receptor by the **HLA-E** class Ib molecule induces SHP-1 phosphatase recruitment to tyrosine-phosphorylated **NKG2**-A. Evidence for receptor function in heterologous transfectants

SO European Journal of Immunology (**1998**), 28(4), 1280-1291
CODEN: EJIMAF; ISSN: 0014-2980

AB It was recently demonstrated that the **CD94/NKG2**-A killer inhibitory receptor (KIR) specifically recognizes the **HLA-E** class Ib mol. The apparent **CD94**-mediated specific recognition of different HLA class Ia allotypes, transfected into the HLA-defective cell line 721.221, indeed depends on their selective ability to concomitantly stabilize the surface expression of endogenous **HLA-E** mols., which confer protection against **CD94/NKG2**-A+ effector cells. The authors show that a selective engagement of the **CD94/NKG2**-A inhibitory receptor with a specific monoclonal antibody (mAb) (Z199) was sufficient to induce Tyr phosphorylation of the **NKG2**-A subunit and SHP-1 recruitment. These early biochem. events, commonly related to neg. signaling pathways, were also detected upon the specific interaction of **NK** cells with an **HLA-E**+ 721.221 transfectant (.221-AEH), and were prevented by pre-incubation of.221-AEH with an anti-HLA class I mAb. MAb crosslinking of the **CD94/NKG2**-A receptor, segregated from other **NK**-assocd. mols. by transfection into a rat basophilic leukemia cell line (RBL-2H3), promoted Tyr phosphorylation of **NKG2**-A and co-pptn. of SHP-1, together

with an inhibition of secretory events triggered via Fc.epsilon.RI. Interaction of **CD94/NKG2**-A+ RBL cells with the **HLA-E**+.221-AEH transfectant specifically induced a detectable assocn. of SHP-1 with **NKG2**-A, constituting a more formal evidence for the receptor-HLA class I interaction.

ST **CD94 NKG2A** phosphorylation **HLA E**; SHP1 phosphatase **CD94 NKG2A** receptor

IT CD antigens
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**CD94**, complexes, with **NKG2**-A; **HLA-E** ligand-induced recruitment of SHP-1 phosphatase to ITIM-phosphorylated **NKG2**-A of killer inhibitory receptor)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HLA, class I, receptors, KIR, **CD94/NKG2**-A; **HLA-E** ligand-induced recruitment of SHP-1 phosphatase to ITIM-phosphorylated **NKG2**-A of killer inhibitory receptor)

IT Signal transduction, biological
(**HLA-E** ligand-induced recruitment of SHP-1 phosphatase to ITIM-phosphorylated **NKG2**-A of killer inhibitory receptor)

IT Histocompatibility antigens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**HLA-E**; **HLA-E** ligand-induced recruitment of SHP-1 phosphatase to ITIM-phosphorylated **NKG2**-A of killer inhibitory receptor)

IT Protein motifs
(ITIM (immunoreceptor tyrosine-based inhibitory motif); **HLA-E** ligand-induced recruitment of SHP-1 phosphatase to ITIM-phosphorylated **NKG2**-A of killer inhibitory receptor)

IT Antigen receptors
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(KIR (killer cell inhibitory), **CD94/NKG2**-A; **HLA-E** ligand-induced recruitment of SHP-1 phosphatase to ITIM-phosphorylated **NKG2**-A of killer inhibitory receptor)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**NKG2**-A, complexes, with **CD94**; **HLA-E** ligand-induced recruitment of SHP-1 phosphatase to ITIM-phosphorylated **NKG2**-A of killer inhibitory receptor)

IT Lymphocyte
(natural killer cell; **HLA-E** ligand-induced recruitment of SHP-1 phosphatase to ITIM-phosphorylated **NKG2**-A of killer inhibitory receptor)

IT Phosphorylation, biological
(receptor; **HLA-E** ligand-induced recruitment of SHP-1 phosphatase to ITIM-phosphorylated **NKG2**-A of killer inhibitory receptor)

IT 79747-53-8, Tyrosine phosphatase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(SHP-1; **HLA-E** ligand-induced recruitment of SHP-1 phosphatase to ITIM-phosphorylated **NKG2**-A of killer inhibitory receptor)

L8 ANSWER 6 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 5
SO Journal of Experimental Medicine (**1998**), 188(5), 973-978
CODEN: JEMEAV; ISSN: 0022-1007
AB . . . binds with high affinity and accounts for almost all of the peptides assocd. with this mol. Human histocompatibility leukocyte antigen (**HLA**)-**E**, a homolog of Qa-1b, binds similar peptides derived from human class Ia mols. and interacts with **CD94/NKG2** receptors on natural killer cells. The authors used surface plasmon resonance to det. the ability of Qa-1b to bind related. . . peptides derived from the leaders of class I mols. from several mammalian species. All of the peptides reported to bind **HLA-E** bound readily to Qa-1b. In addn., peptides derived from leader segments of different mammals also bound to Qa-1b, indicating a. . .

L8 ANSWER 7 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 6
TI Recognition of human histocompatibility leukocyte antigen (**HLA**)-**E** complexed with HLA class I signal sequence-derived peptides by **CD94/NKG2** confers protection from natural killer cell-mediated lysis
SO Journal of Experimental Medicine (**1998**), 187(5), 813-818
CODEN: JEMEAV; ISSN: 0022-1007
AB Human histocompatibility leukocyte antigen (**HLA**)-**E** is a nonclassical HLA class I mol., the gene for which is transcribed in most tissues. It has recently been. . . reported that this mol. binds peptides derived from the signal sequence of HLA class I proteins; however, no function for **HLA-E** has yet been described. The authors show that natural killer (**NK**) cells can recognize target cells expressing **HLA-E** mols. on the cell surface and this interaction results in inhibition of the lytic process. Furthermore, **HLA-E** recognition is mediated primarily through the **CD94/NKG2**-A heterodimer, as **CD94**-specific, but not killer cell inhibitory receptor (KIR)-specific mAbs block **HLA-E**-mediated protection of target cells. Cell surface **HLA-E** could be increased by incubation with synthetic peptides corresponding to residues 3-11 from the signal sequences of a no. of. . . HLA class I mols.; however, only peptides which contained a Met at position 2 were capable of conferring resistance to **NK**-mediated lysis, whereas those having Thr at position 2 had no effect. Interestingly, HLA class I mols. previously correlated with **CD94/NKG2** recognition all have Met at residue 4 of the signal sequence (position 2 of the **HLA-E** binding peptide), whereas those which have been reported not to interact with **CD94/NKG2** have Thr at this position. These data thus show a function for **HLA-E** and suggest an alternative explanation for the apparent broad reactivity of **CD94/NKG2** with HLA class I mols.; that **CD94/NKG2** interacts with **HLA-E** complexed with signal sequence peptides derived from "protective" HLA class I alleles rather than directly interacting with classical HLA class. . .

IT Receptors

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**CD94/NKG2**; recognition of **HLA-E** complexed with HLA class I signal sequence-derived peptides by **CD94/NKG2** confers protection from natural killer cell-mediated lysis)

IT CD antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**CD94**; recognition of **HLA-E** complexed with HLA class I signal sequence-derived peptides by **CD94/NKG2** confers protection from natural killer cell-mediated lysis)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HLA, class I; recognition of **HLA-E** complexed with HLA class I signal sequence-derived peptides by **CD94/NKG2** confers protection from natural killer cell-mediated lysis)

IT Histocompatibility antigens
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**HLA-E**; recognition of **HLA-E** complexed with HLA class I signal sequence-derived peptides by **CD94/NKG2** confers protection from natural killer cell-mediated lysis)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**NKG2**; recognition of **HLA-E** complexed with HLA class I signal sequence-derived peptides by **CD94/NKG2** confers protection from natural killer cell-mediated lysis)

IT Lymphocyte
(natural killer cell; recognition of **HLA-E** complexed with HLA class I signal sequence-derived peptides by **CD94/NKG2** confers protection from natural killer cell-mediated lysis)

IT Cytolysis
(recognition of **HLA-E** complexed with HLA class I signal sequence-derived peptides by **CD94/NKG2** confers protection from natural killer cell-mediated lysis)

IT 193002-77-6 202657-62-3 202657-64-5 205491-11-8
RL: PRP (Properties)
(recognition of **HLA-E** complexed with HLA class I signal sequence-derived peptides by **CD94/NKG2** confers protection from natural killer cell-mediated lysis)

L8 ANSWER 8 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 7

TI **HLA-E** binds to natural killer cell receptors **CD94/NKG2A**, B and C

SO Nature (London) (**1998**), 391(6669), 795-799
CODEN: NATUAS; ISSN: 0028-0836

AB The protein **HLA-E** is a non-classical major histocompatibility complex (MHC) mol. of limited sequence variability. Its expression on the cell surface is regulated. . . derived from the signal sequence of some other MHC class I mols. Here we report the identification of ligands for **HLA-E**. We constructed tetramers in which recombinant **HLA-E** and .beta.2-microglobulin were refolded with an MHC, leader-sequence peptide, biotinylated, and conjugated to phycoerythrin-labeled Extravidin. This **HLA-E** tetramer bound to natural killer (**NK**) cells and a small subset of T cells from peripheral blood. On transfectants, the tetramer bound to the **CD94/NKG2A**, **CD94/NKGK2B** and **CD94/NKG2C** NM cell receptors, but did not bind to the Ig family of **NK** cell receptors (KIR). Surface expression of **HLA-E** was enough to protect target cells from lysis by **CD94/NKG2A** + **NK**-cell clones. A subset of HLA class I alleles has been shown to inhibit killing by **CD94/NKG2A**+ **NK** -cell clones. Only the HLA alleles that posses a leader peptide capable of upregulating **HLA-E** surface expression confer resistance to **NK**-cell-mediated lysis, implying that their action is mediated by **HLA-E**, the predominant ligand for the **NK** cell inhibitory receptor **CD94/NKG2A**.

ST **HLA E** natural killer cell receptor; **CD94** **NKG2** receptor natural killer cell

IT CD antigens
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(**CD94**; **HLA-E** antigen binding to natural killer cell receptors **CD94/NKG2A**, B and C and resistance to **NK**-mediated lysis)

IT Histocompatibility antigens
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(HLA, class I, alleles; **HLA-E** antigen binding to natural killer cell receptors **CD94/NKG2A**, B and C and resistance to **NK**-mediated lysis by leader peptides from)

IT Cytolysis
(**HLA-E** antigen binding to natural killer cell receptors **CD94/NKG2A**, B and C and resistance to **NK**-mediated lysis)

IT Histocompatibility antigens
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(**HLA-E**; **HLA-E** antigen binding to natural killer cell receptors **CD94/NKG2A**, B and C and resistance to **NK**-mediated lysis)

IT Antigen receptors
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(**NKG2**, variants A and B and C; **HLA-E** antigen binding to natural killer cell receptors **CD94/NKG2A**, B and C and resistance to **NK**-mediated lysis)

IT Lymphocyte
(natural killer cell; **HLA-E** antigen binding to natural killer cell receptors **CD94/NKG2A**, B and C

and resistance to **NK**-mediated lysis)

L8 ANSWER 9 OF 30 CAPLUS COPYRIGHT 2002 ACS
SO Cell (Cambridge, Massachusetts) (**1998**), 92(6), 705-707
CODEN: CELLB5; ISSN: 0092-8674
AB . . . . discussing the function of mouse Ly49 receptors, the structure and function of human KIR receptors, and the mol. interaction of **HLA-E** with **CD94/NKG2** heterodimers.
IT Histocompatibility antigens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**HLA-E**; structure and function of **NK** cell receptors for classical and nonclassical MHC class I)

L8 ANSWER 10 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 8
SO Immunity (**1998**), 8(6), 693-701
CODEN: IUNIEH; ISSN: 1074-7613
AB While the inhibitory **NK** cell receptors for MHC class I express immunoreceptor tyrosine-based inhibitory motifs that recruit intracellular tyrosine phosphatases and prevent **NK** cell effector function, the activating **NK** cell receptors lack intrinsic sequences required for cellular stimulation. **CD94/NKG2C**, an activating **NK** cell receptor of the C-type lectin superfamily that binds to **HLA-E**, noncovalently assocs. with DAP12, a membrane receptor contg. an immunoreceptor tyrosine-based activating motif. Efficient expression of **CD94/NKG2C** on the cell surface requires the presence of DAP12, and charged residues in the transmembrane domains of DAP12 and **NKG2C** are necessary for this interaction. These results provide a mol. basis for the assembly of **NK** cell receptors for MHC class I involved in cellular activation and inhibition.
IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(**HLA-E**, receptors, **CD94/NKG2C**; DAP12 protein assocn. with activating **CD94/NKG2C** **NK** cell receptors)

L8 ANSWER 11 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 9
SO Molecular Cell (**1998**), 1(4), 531-541
CODEN: MOCEFL; ISSN: 1097-2765
AB The crystal structure of the nonclassical human class Ib MHC mol. **HLA-E** has been detd. in complex with a prototypic ligand, the nonamer peptide (VMAPRTVLL), derived from the highly conserved residues 3-11. . . . of peptide binding retains some of the std. features obsd. in MHC class Ia complexes, but novel features imply that **HLA-E** has evolved to mediate specific binding to a tightly defined set of almost identical hydrophobic peptides from the highly conserved class I leader sequences. These mol. adaptations make **HLA-E** a rigorous checkpoint at the cell surface reporting on the integrity of the antigen processing pathway to **CD94/NKG2** receptor-bearing natural killer cells.
IT CD antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(**CD94**, -**NKG2** receptors; structural features impose tight peptide binding specificity in the nonclassical MHC mol. **HLA-E** and natural killer cell)
IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(**HLA-E**, complexes with peptides and **CD94/NKG2** receptors; structural features impose tight peptide binding specificity in the nonclassical MHC mol. **HLA-E**)
IT Antigen receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(**NKG2/CD94** complex; structural features impose tight peptide binding specificity in the nonclassical MHC mol. **HLA-E** and natural killer cell)

L8 ANSWER 12 OF 30 CAPLUS COPYRIGHT 2002 ACS
SO Periodicum Biologorum (**1998**), 100(4), 441-443
CODEN: PDBIAD; ISSN: 0031-5362
IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**HLA-E**; recognition by **CD94/NKG2** heterodimers of human natural killer cells)

L8 ANSWER 13 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 10
TI **HLA-E** is the ligand for the natural killer cell **CD94/NKG2** receptors
SO Journal of Biomedical Science (Basel) (**1998**), 5(5), 321-331
CODEN: JBCIEA; ISSN: 1021-7770
AB A review is given with 102 refs. **CD94/NKG2** is a recently described receptor present on natural killer (**NK**) cells and certain T cells that is composed of the **CD94** chain covalently assocd. with a member of the **NKG2** family of mols. Both chains are glycosylated members of the C-type lectin superfamily. The **CD94/NKG2** receptors are functionally heterogeneous depending on which **NKG2** family member is assocd. with **CD94**. It was thought that **CD94/NKG2** receptors recognized a broad array of HLA-A, -B, and -C (classical), as well as the nonclassical HLA-G, MHC class I mols. Recent data have suggested that this receptor is specific for **HLA-E** complexed with a peptide derived from the signal sequence (residues 3-11) of certain classical MHC class I mols. Position 2 (residue 4) in the signal sequence derived peptides appears pivotal in detg. whether the **HLA-E**/peptide complex confers resistance to **NK**-mediated lysis. The potential roles that the **CD94/NKG2-HLA-E** receptor ligand interaction might play in infection and tumor development are discussed.
IT CD antigens
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**CD94**; **HLA-E**, ligand for the natural killer cell **CD94/NKG2** receptors)
IT Histocompatibility antigens
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological

study); OCCU (Occurrence)
(**HLA**; **HLA-E**, ligand for the natural killer cell **CD94/NKG2** receptors)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**NKG2**; **HLA-E**, ligand for the natural killer cell **CD94/NKG2** receptors)

IT Lymphocyte
(natural killer cell; **HLA-E**, ligand for the natural killer cell **CD94/NKG2** receptors)

L8 ANSWER 14 OF 30 CAPLUS COPYRIGHT 2002 ACS
SO Immunity (**1998**), 9(3), 289-294
CODEN: IUNIEH; ISSN: 1074-7613
AB A review with 50 refs. This paper discusses how recognition of **HLA-E** enables **NK** cells to monitor the integrity of the MHC class I-dependent antigen presentation pathway. Since certain subpopulations of activated cytotoxic T cells (CTLs) can also express the **HLA-E**-recognizing inhibitory receptors, exptl. results are described regarding the effects of inhibitory receptors on CTL activation. Finally, the potential implications of **HLA-E** recognition on antitumor immunity, antiviral immunity, and materno-fetal interactions are discussed.
ST review cytotoxic lymphocyte **HLA E CD94 NKG2**
IT CD antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**CD94**; cytotoxic lymphocyte recognition of **HLA-E**)
IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**NKG2**; cytotoxic lymphocyte recognition of **HLA-E**)

L8 ANSWER 15 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 11
SO Immunological Reviews (**1998**), 163, 129-138
CODEN: IMRED2; ISSN: 0105-2896
AB A review with 49 refs. The major histocompatibility (MHC) class Ib mols. **HLA-E**, **HLA**-F and HLA-G are relatively non-polymorphic compared to class Ia mols. Both **HLA-E** and **HLA**-G bind peptides and are involved in natural killer (**NK**)-cell recognition, but the role of HLA-F is unclear. **HLA-E** binds specifically to the conserved leader sequence peptides from the class Ia MHC mols. and interacts on the cell surface with the **CD94/NKG2** class of **NK**-cell receptors. The framework structure of **HLA-E** is similar to that of the MHC class Ia mols., but the peptide-binding groove is highly adapted for the specific. . . binding of the leader sequence peptides. This is different from class Ia mols., which have highly promiscuous peptide-binding grooves. The **HLA-E** groove makes full use of all the available pockets and imposes specificity along the entire length of the peptide. HLA-G. . . with leucine or isoleucine at position 2, proline at position 3 and leucine at position 9. Expression of HLA-G inhibits **NK** cells expressing the **CD94/NKG2** class of receptors, though an interaction with these receptors has not been directly demonstrated.
IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**CD94**; structure and function of human MHC class Ib mols. **HLA-E**, **HLA**-F and HLA-G)

L8 ANSWER 16 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI **HLA-E**-bound peptides influence recognition by inhibitory and triggering **CD94/NKG2** receptors: Preferential response to an HLA-G-derived nonamer.
SO Natural Immunity, (**Feb., 1998**) Vol. 16, No. 2-3, pp. 80. Meeting Info.: Fifth Annual Meeting of the Society for Natural Immunity Seventeenth International. . .
IT Major Concepts
Immune System (Chemical Coordination and Homeostasis)
IT Chemicals & Biochemicals
CD94/NKG2 receptors; **HLA-E**-bound peptides; HLA-G-derived nonamers

L8 ANSWER 17 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI Decidual **NK** cells have receptors for **HLA-E** which is expressed by human trophoblast.
SO Natural Immunity, (**Feb., 1998**) Vol. 16, No. 2-3, pp. 79. Meeting Info.: Fifth Annual Meeting of the Society for Natural Immunity Seventeenth International. . .

L8 ANSWER 18 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI Specific recognition of **HLA-E** but not classical HLA class I molecules by soluble **CD94/NKG2A** and **NK** cells.
SO Natural Immunity, (**Feb., 1998**) Vol. 16, No. 2-3, pp. 72. Meeting Info.: Fifth Annual Meeting of the Society for Natural Immunity Seventeenth International. . .
IT . . .
Parts, Structures, & Systems of Organisms
NK cell [natural killer cell]: blood and lymphatics, immune system
IT Chemicals & Biochemicals
CD94; **CD94/NKG2A** complex; HLA class I molecules; **HLA-E**: recognition; **NKG2A**

L8 ANSWER 19 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI **NK** cell-mediated recognition of **HLA-E** and **HLA**-G class Ib molecules.
SO Natural Immunity, (**Feb., 1998**) Vol. 16, No. 2-3, pp. 71. Meeting Info.: Fifth Annual Meeting of the Society for Natural Immunity Seventeenth International. . .
IT . . .
Parts, Structures, & Systems of Organisms
NK cell [natural killer cell]: blood and lymphatics, immune system
IT Chemicals & Biochemicals
CD94; **CD94/NKG2A** complex; **HLA-E** class Ib molecules; HLA-G class Ib molecules; **NKG2A**

; SHP1 tyrosine phosphatase

L8 ANSWER 20 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 12
SO Tissue Antigens (1997), 50(6), 695-698
CODEN: TSANA2; ISSN: 0001-2815
AB . . . . has also been found in both Cercopithecinae and humans. These allelic and evolutionary data suggest an altogether different functionality for **HLA-E** (and also HLA-G) compared with classical class I proteins: i.e., sending neg. (tolerogenic) signals to **NK** and T cells.

L8 ANSWER 21 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 13
SO Journal of Experimental Medicine (1997), 185(3), 385-391
CODEN: JEMEAV; ISSN: 0022-1007
AB . . . . -B, and -C, is the presentation of peptides to T cells. A second function is the inhibition of natural killer (**NK**) cells, mediated by binding of class I mols. to **NK** receptors. In contrast, the function of the nonclassical human MHC class I mols., **HLA-E**, -F, and -G, is still a mystery. The specific expression of HLA-G in placental trophoblast suggests an important role for. . . . escapes maternal allorecognition by downregulation of HLA-A and HLA-B mols. at this interface. It has been suggested that the maternal **NK** recognition of this downregulation is balanced by the expression of HLA-G, thus preventing damage to the placenta. Here, we describe the partial inhibition of **NK** lysis of the MHC class I neg. cell line LCL721.221 upon HLA-G transfection. We present three **NK** lines that are inhibited via the interaction of their **NKAT3** receptor with HLA-G and with HLA-Bw4 mols. Inhibition can be blocked by the anti-**NKAT3** antibody 5.133. In conclusion, **NK** inhibition by HLA-G via **NKAT3** may contribute to the survival of the fetal semiallograft in the mother during pregnancy.

L8 ANSWER 22 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
SO Placenta, (1997) Vol. 18, No. 2-3, pp. 234-235.
ISSN: 0143-4004.
IT Miscellaneous Descriptors
BLOOD AND LYMPHATICS; CD4-POSITIVE CELL; CD8-POSITIVE CELL; **CD94**; HLA-DQ; HLA-DR; **HLA-E**; HLA-G; IMMUNE SYSTEM; INTERFERON-GAMMA; INTERLEUKIN-3; INTERLEUKIN-5; KILLER INHIBITORY RECEPTORS; LARGE GRANULAR LYMPHOCYTES; MAJOR HISTOCOMPATIBILITY COMPLEX; PEPTIDE INTERACTIONS; P58; RECURRENT SPONTANEOUS. . .

L8 ANSWER 23 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 14
SO Medecine/Sciences, (1996) 12/11 (1209-1218).
ISSN: 0767-0974 CODEN: MSMSE4
AB . . . encode membrane-anchored cell surface glycoproteins that present the endogenous antigenic peptides to the T cell receptors and are recognized by **NK** cell receptors. These genes are characterized by a high polymorphism and a nearly ubiquitous expression. The biological function of the three nonclassical class I genes **HLA-E**, **HLA**-F, and HLA-G still remains uncertain. In addition to these six genes, the MHC contains a number of class I pseudoaenes. . .

L8 ANSWER 24 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 15
SO J. Exp. Med. (1994), 180(2), 537-43
CODEN: JEMEAV; ISSN: 0022-1007
AB Natural killer (**NK**) cells kill normal and transformed hematopoietic cells that lack expression of major histocompatibility complex (MHC) class I antigens. Lysis of HLA-neg. Epstein Barr virus-transformed B lymphoblastoid cell lines (B-LCL) by human **NK** cell clones can be inhibited by transfection of the target cells with certain HLA-A, -B, or -C alleles. **NK** cell clones established from an individual demonstrate clonal heterogeneity in HLA recognition and a single **NK** clone can recognize multiple alleles. The authors describe a potential human **NK** cell receptor (**NKB1**) for certain HLA-B alleles (e.g., **HLA**-B*5101 and -B*5801) identified by the mAb DX9. **NKB1** is a 70 kDa glycoprotein that is expressed on a subset of **NK** cells and **NK** cell clones. DX9 monoclonal antibody (mAb) specifically inhibits the interaction between **NK** cell clones and B-LCL targets transfected with certain HLA-B alleles, but does not affect recognition of HLA-A or HLA-C antigens. An individual **NK** cell clone can independently recognize B-LCL targets transfected with HLA-B or HLA-C antigens; however, DX9 mAb only affects interaction with transfectants expressing certain HLA-B alleles. These findings demonstrate the existence of **NK** cell receptors involved in the recognition of HLA-B and imply the presence of multiple receptors for MHC on an individual **NK** clone.

L8 ANSWER 25 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 16
SO Proc. Natl. Acad. Sci. U. S. A. (1992), 89(17), 8337-41
CODEN: PNASA6; ISSN: 0027-8424
AB Target structures important for natural killer (**NK**) cell recognition of virally infected cells are not well defined. Since major histocompatibility complex (MHC) class I mols. bind viral. . . acute infection, it was evaluated whether an interaction between MHC and virus might influence the susceptibility of infected cells to **NK** cell-mediated lysis. To control for MHC class I expression on target cells, either HLA class I-deficient C1R cells or C1R sublines expressing transfected HLA class I gene products were used. Human **NK** cells were unable to preferentially lyse class I-deficient C1R cells after infection with herpes simplex virus (HSV). In contrast, HLA class I transfectants were more susceptible to **NK** cell-mediated cytotoxicity after HSV infection. This occurred for HSV-infected C1R cells expressing any of the 3 HLA class I gene products tested (i.e., **HLA**-B27, HLA-A3, or HLA-Aw68), indicating that **NK** cells recognition in this system does not require self MHC and is not unique for a single haplotype. Productive HSV. . . the target structures on HSV-infected, HLA class I+ targets. These results demonstrate a role for MHC class I in regulating **NK** cell-mediated killing of virus-infected cells.

L8 ANSWER 26 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 17
SO Journal of Immunology, (1992) 148/2 (627-632).
ISSN: 0022-1767 CODEN: JOIMA3
AB . . . designated EO15 has been isolated and found to encode a non-classical HLA class I gene transcript. EO15 was compared with **HLA-E** and found to be 99.9% similar at the nucleotide level and to extend further in the 3' untranslated region. The. . . EO15 3' end suggests that EO15 clone represents a copy of the 3.3-kb mRNA species detected in Northern blot analyses. **HLA-E** transcripts of 1.9 and 3.3 kb have been described in a variety of cell

types. The two EO15 mRNA species, similar in size to the previously defined **HLA-E** mRNA, were present at high levels in blood leukocyte populations and at variable levels in different cell lines. The EO15. . . of EO15 transcripts were detected in B and monocytic cell lines, whereas intermediate and lower levels were found in eosinophilic, **NK**-like, megakaryocytic, and T cell lines, respectively. Similar to its effect on classical HLA class I transcripts, IFN-.gamma. increased the levels. . . mRNA in eosinophils and neutrophils from hypereosinophilic patients. These results suggest that purified blood eosinophils as well as neutrophils express EO15/**HLA** -**E** mRNA; however, further experiments are needed to investigate the localization and the function of EO15 protein products.

L8 ANSWER 27 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
SO International Archives of Allergy and Immunology, (**1992**) 99/2-4 (230-233).
ISSN: 1018-2438 CODEN: IAAIEG
AB This paper reviews recent progresses on human Natural Killer (**NK**) cells which profoundly changed our concepts on **NK** cells and their functions. Regarding the ontogeny of **NK** cells, immature thymocyte populations (CD-3-4-16-) have been shown to give rise to **NK** cells, provided suitable culture conditions. This indicates that precursor potentially capable of differentiation towards the **NK** cell lineage are present within the human thymus. Although **NK** cells lack known receptors for antigen (i.e. sIg and TCR), **NK** cell populations or clones were found to be capable of mediating specific recognition of allogenic cells. This specific function was clonally distributed and, more importantly, **NK** clones displaying different patterns of allospecificity could be isolated from single individuals. These data indicate the existence of a **NK** cell repertoire for alloantigen recognition. Analysis of the surface molecules identified by **NK** cells indicated that certain **HLA** alleles (e.g. **HLA**-Cw3) can act as specific protective elements from lysis by clones with defined specificities (e.g. specificity 2). Therefore, HLA class I molecules appear to play a central role in the **NK** cell-mediated functions. The finding that human **NK** cells express a clonally-dystributed ability to recognize alloantigens suggested the existence of distinct surface receptors. Indeed, a new family of. . . the use of monoclonal antibodies. The expression of these molecules was shown to represent a stable phenotipic property of human **NK** cells and to be clonally distributed. More importantly, the expression of 58 kD molecules appears to correlate with the ability. . . given allospecificities. These data are supporting the concept that 58 kD molecules are part of receptor structures involved in the **NK** cell-mediated recognition.

L8 ANSWER 28 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 18
SO Journal of Experimental Medicine, (**1990**) 171/4 (1315-1332).
ISSN: 0022-1007 CODEN: JEMEAV
AB . . . absence of CD4+ helper T cells and are not inhibited by anti-CD4 mAb. Both antigen-specific CTL as well as nonspecific **NK** cells can be elicited by dendritic cells. The **NK** cell response can be depleted at the precursor level by panning with an anti-CD11b mAb, which removes a CD11b+/CD28-, CD16+. . . have been sensitized by dendritic cells. The number of CD8+ cells that are blast transformed and express an activated phenotype (i.e., **HLA** DR/DQ+, CD25/IL-2R+, CD45R-) reaches 30-40% of the culture at day 4-5, the peak of the helper-independent response. We conclude that. . .

L8 ANSWER 29 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 19
SO Journal of Clinical Investigation, (**1989**) 83/1 (278-287).
ISSN: 0021-9738 CODEN: JCINAO
AB The role of major histocompatibility gene products (i.e., **HLA** molecules) in rendering tumor cells resistant to natural killer (**NK**) cell-mediated lysis was investigated by using mouse monoclonal antibodies to bind and mask HLA or non-HLA gene products on the. . . tumor targets. Enhanced lysis was not due to antibody dependent cellular cytotoxicity or due to an effect of antibody on **NK** effectors. Of importance, normal autologous and allogeneic human lymphocytes could not be lysed by **NK** cells despite blast transformation with mitogens or masking of HLA membrane determinants on blasts with monoclonal antibodies. Enhanced lysis, in the presence of antibody to HLA antigens, was not due to increased **NK** cell binding to tumor targets, but a consequence of enhanced postbinding lysis. Studies using granules obtained from **NK** cells indicated that masking of HLA antigens did not enhance the susceptibility of tumor targets to cytolysis. Such observations would. . . HLA antigens on tumor targets inhibit the triggering of effector cells (and release of cytolysins) after recognition and binding of **NK** cells to target cells.

L8 ANSWER 30 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 20
SO Wiener Klinische Wochenschrift, (**1987**) 99/24 (848-855).
ISSN: 0043-5325 CODEN: WKWOAO
AB . . . in conjunction with BAL provides further differentiation of lymphocytes into T- and B-, T-helper and T-suppressor types, natural killer cells (**NK** cells) and cytotoxic T-cells. A predominance of T-suppressor lymphocytes is an indication of EAA, whereas a predominance of T-helper lymphocytes is positively correlated with sarcoidosis. Other markers, e.g. **HLA**-DR, when expressed on the surface of alveolar macrophages, merely indicate activation unrelated to a specific type of lymphocytic alveolitis. BAL. . .

=> dis his

(FILE 'HOME' ENTERED AT 13:53:22 ON 24 JUN 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 13:53:34 ON 24 JUN 2002
L1 3511 S BRAUD V?/AU OR ALLAN D?/AU OR OGG G?/AU OR OCALLAGHAN C?/AU O
L2 47 S L1 AND (NK?)
L3 35 S L2 AND (HLA (1N) E)
L4 14 DUP REM L3 (21 DUPLICATES REMOVED)
L5 72958 S NK (P) (NK? OR CD94?)
L6 315 S (HLA (1N) E) (P) (NK? OR CD94?)
L7 63 S L6 AND PD<19981204
L8 30 DUP REM L7 (33 DUPLICATES REMOVED)

=> dis l8 1-30 ibib abs

L8 ANSWER 1 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
ACCESSION NUMBER: 1998:289045 CAPLUS

DOCUMENT NUMBER: 129:66613
TITLE: **HLA-E** is a major ligand for the natural killer inhibitory receptor **CD94/NKG2A**
AUTHOR(S): Lee, Ni; Llano, Manuel; Carretero, Marta; Ishitani, Akiko; Navarro, Francisco; Lopez-Botet, Miguel; Geraghty, Daniel E.
CORPORATE SOURCE: The Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA, 98104-2092, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (**1998**), 95(9), 5199-5204
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors previously showed that the availability of a nonamer peptide derived from certain HLA class I signal sequences is a necessary requirement for the stabilization of endogenous **HLA-E** expression on the surface of 721.221 cells. This led the authors to examine the ability of **HLA-E** to protect HLA class I transfectants from natural killer (**NK**) cell-mediated lysis. It was possible to implicate the **CD94/NKG2A** complex as an inhibitory receptor recognizing this class Ib mol. by using as target a .221 transfectant selectively expressing surface **HLA-E** . **HLA-E** had no apparent inhibitory effect mediated through the identified Ig superfamily (Ig-SF) human killer cell inhibitory receptors or ILT2/LIR1. Further studies of **CD94/NKG2+** **NK** cell-mediated recognition of .221 cells transfected with different HLA class I allotypes (i.e., -Cw4, -Cw3, -B7) confirmed that the inhibitory interaction was mediated by **CD94/NKG2A** recognizing the surface **HLA-E** mol., because only antibodies directed against either **HLA-E**, **CD94** , or **CD94/NKG2A** specifically restored lysis. Surface stabilization of **HLA-E** in cold-treated .221 cells loaded with appropriate peptides was sufficient to confer protection, resulting from recognition of the HLA class Ib mol. by the **CD94/NKG2A** inhibitory receptor. Consistent with the prediction that the ligand for **CD94/NKG2A** is expressed ubiquitously, the authors' examn. of **HLA-E** antigen distribution indicated that it is detectable on the surface of a wide variety of cell types.

L8 ANSWER 2 OF 30 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:288970 CAPLUS
DOCUMENT NUMBER: 129:66532
TITLE: HLA class I specificity for natural killer cell receptor CD94NKG2A: two for one in more ways than one
AUTHOR(S): Yokoyama, Wayne M.
CORPORATE SOURCE: Howard Hughes Medical Institute, Rheumatology Division, Washington University School of Medicine, St. Louis, MO, 63110, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (**1998**), 95(9), 4791-4794
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review and discussion with 44 refs. There are abundant data to substantiate the conclusion that **CD94/NKG2A** receptors of human natural killer cells directly recognize **HLA-E** mols.

L8 ANSWER 3 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
ACCESSION NUMBER: 1998:800568 CAPLUS
DOCUMENT NUMBER: 130:64947
TITLE: The Qa-1b molecule binds to a large subpopulation of murine NK cells
AUTHOR(S): Salcedo, Margarita; Bousso, Philippe; Ljunggren, Hans-Gustaf; Kourilsky, Philippe; Abastado, Jean-Pierre
CORPORATE SOURCE: Unite Biologie Moleculaire Gene, Institut Pasteur, Paris, F-75015, Fr.
SOURCE: European Journal of Immunology (**1998**), 28(12), 4356-4361
CODEN: EJIMAF; ISSN: 0014-2980
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Recent studies on human **NK** cells have demonstrated that the **NK** cell **CD94/NKG2** receptors bind to the nonclassical MHC class I mol. **HLA-E**. A functional **CD94/NKG2** complex has not yet been identified in rodents, but cDNA encoding rat and mouse **CD94** and **NKG2** have recently been cloned, suggesting that **CD94/NKG2** receptors may exist in species other than man. The mouse nonclassical MHC class I mol. Qa-1 shares several features with **HLA-E**. This suggests that Qa-1 may be similarly recognized by murine **NK** cells. To study the ability of Qa-1 to bind to murine **NK** cells, the authors have produced a sol. tetrameric form of Qa-1b. The authors demonstrate that Qa-1b tetramers distinctly bind to a large subset of fresh or IL-2-activated **NK1.1+**/CD3- splenocytes independently of the expression of Ly49 inhibitory receptors. Binding occurs whether **NK** cells have evolved in an MHC class I-expressing or in an MHC class I-deficient environment. The data suggest the existence of a Qa-1-recognizing structure on a large subpopulation of murine **NK** cells that may be similar to the human **CD94/NKG2** heterodimeric complex.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
ACCESSION NUMBER: 1998:612269 CAPLUS
DOCUMENT NUMBER: 130:1528
TITLE: **HLA-E**-bound peptides influence recognition by inhibitory and triggering **CD94/NKG2** receptors. Preferential response to an HLA-G-derived nonamer
AUTHOR(S): Llano, Manuel; Lee, Ni; Navarro, Francisco; Garcia, Pilar; Albar, Juan Pablo; Geraghty, Daniel E.; Lopez-Botet, Miguel

CORPORATE SOURCE: Servicio Immunologia, Hospital Princesa, Madrid, E-28006, Spain
SOURCE: European Journal of Immunology (1998), 28(9), 2854-2863
CODEN: EJIMAF; ISSN: 0014-2980
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The **HLA-E** class Ib mol. constitutes a major ligand for the lectin-like **CD94/NKG2** natural killer (**NK**) cell receptors. Specific HLA class I leader sequence-derived nonapeptides bind to endogenous **HLA-E** mols. in the HLA-defective cell line 721.221, inducing **HLA-E** surface expression, and promote **CD94/NKG2A**-mediated recognition. The authors compared the ability of **NK** clones which expressed either inhibitory or activating **CD94/NKG2** receptors to recognize **HLA-E** mols. on the surface of 721.221 cells loaded with a panel of synthetic nonamers derived from the leader sequences of most HLA class I mols. The results support the notion that the primary structure of the **HLA-E**-bound peptides influences **CD94/NKG2**-mediated recognition, beyond their ability to stabilize surface **HLA-E**. **CD94/NKG2A+ NK** clones appeared more sensitive to the interaction with most **HLA-E**-peptide complexes than did effector cells expressing the activating **CD94/NKG2C** receptor. An exception to this pattern was I-ILA-E loaded with the HLA-G-derived nonamer. This complex triggered cytotoxicity very efficiently over a wide range of peptide concns., suggesting that the **HLA-E**/G-nonamer complex interacts with the **CD94/NKG2** triggering receptor with a higher affinity. These results raise the possibility that **CD94/NKG2**-mediated recognition of **HLA-E** expressed on extravillous cytotrophoblasts plays an important role in maternal-fetal cellular interactions.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 4
ACCESSION NUMBER: 1998:231442 CAPLUS
DOCUMENT NUMBER: 129:3692
TITLE: Specific engagement of the **CD94/NKG2**-A killer inhibitory receptor by the **HLA-E** class Ib molecule induces SHP-1 phosphatase recruitment to tyrosine-phosphorylated **NKG2**-A. Evidence for receptor function in heterologous transfectants
AUTHOR(S): Carretero, Marta; Palmieri, Gabriella; Llano, Manuel; Tullio, Valentino; Santoni, Angela; Geraghty, Daniel E.; Lopez-Botet, Miguel
CORPORATE SOURCE: Servicio Immunologia, Hospital Princesa, Universidad Autonoma Madrid, Madrid, E-28006, Spain
SOURCE: European Journal of Immunology (1998), 28(4), 1280-1291
CODEN: EJIMAF; ISSN: 0014-2980
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB It was recently demonstrated that the **CD94/NKG2**-A killer inhibitory receptor (KIR) specifically recognizes the **HLA-E** class Ib mol. The apparent **CD94**-mediated specific recognition of different HLA class Ia allotypes, transfected into the HLA-defective cell line 721.221, indeed depends on their selective ability to concomitantly stabilize the surface expression of endogenous **HLA-E** mols., which confer protection against **CD94/NKG2**-A+ effector cells. The authors show that a selective engagement of the **CD94/NKG2**-A inhibitory receptor with a specific monoclonal antibody (mAb) (Z199) was sufficient to induce Tyr phosphorylation of the **NKG2**-A subunit and SHP-1 recruitment. These early biochem. events, commonly related to neg. signaling pathways, were also detected upon the specific interaction of **NK** cells with an **HLA-E**+ 721.221 transfectant (.221-AEH), and were prevented by pre-incubation of.221-AEH with an anti-HLA class I mAb. MAb crosslinking of the **CD94/NKG2**-A receptor, segregated from other **NK**-assocd. mols. by transfection into a rat basophilic leukemia cell line (RBL-2H3), promoted Tyr phosphorylation of **NKG2**-A and co-pptn. of SHP-1, together with an inhibition of secretory events triggered via Fc.epsilon.RI. Interaction of **CD94/NKG2**-A+ RBL cells with the **HLA-E**+.221-AEH transfectant specifically induced a detectable assocn. of SHP-1 with **NKG2**-A, constituting a more formal evidence for the receptor-HLA class I interaction.

L8 ANSWER 6 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 5
ACCESSION NUMBER: 1998:602367 CAPLUS
DOCUMENT NUMBER: 129:301413
TITLE: Qa-1b binds conserved class I leader peptides derived from several mammalian species
AUTHOR(S): Kurepa, Zoran; Hasemann, Charles A.; Forman, James
CORPORATE SOURCE: Immunology Graduate Program, University of Texas Southwestern Medical Center at Dallas, Dallas, TX, 75235, USA
SOURCE: Journal of Experimental Medicine (1998), 188(5), 973-978
CODEN: JEMEAV; ISSN: 0022-1007
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Qa-1b binds a peptide (AMAPRTLLL), referred to as Qdm (for Qa-1 determinant modifier), derived from the signal sequence of murine class Ia mols. This peptide binds with high affinity and accounts for almost all of the peptides assocd. with this mol. Human histocompatibility leukocyte antigen (**HLA**)-**E**, a homolog of Qa-1b, binds similar peptides derived from human class Ia mols. and interacts with **CD94/NKG2** receptors on natural killer cells. The authors used surface plasmon resonance to det. the ability of Qa-1b to bind related ligands representing peptides derived from the leaders of class I mols. from several mammalian species. All of the peptides reported to bind **HLA-E** bound readily to Qa-1b. In addn., peptides derived from leader segments of different mammals also bound to Qa-1b, indicating a conservation of this "Qdm-like" epitope throughout mammalian evolution. The authors have attempted to define a minimal peptide on a polyglycine backbone that binds Qa-1b. Previous findings showed that P2

and P9 are important but not sufficient for binding to Qa-1b. Although a min. peptide (GMGGGGLLL) bound Qa-1b, its interaction was relatively weak, as were peptides sharing five or six residues with Qdm, indicating that multiple native residues are required for a strong interaction. This finding is consistent with the observation that this mol. preferentially binds this single ligand.

L8 ANSWER 7 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 6
ACCESSION NUMBER: 1998:162486 CAPLUS
DOCUMENT NUMBER: 128:281696
TITLE: Recognition of human histocompatibility leukocyte antigen (**HLA**)-**E** complexed with HLA class I signal sequence-derived peptides by **CD94/NKG2** confers protection from natural killer cell-mediated lysis
AUTHOR(S): Borrego, Francisco; Ulbrecht, Matthias; Weiss, Elisabeth H.; Coligan, John E.; Brooks, Andrew G.
CORPORATE SOURCE: Laboratory of Molecular Structure, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Rockville, MD, 20852, USA
SOURCE: Journal of Experimental Medicine (**1998**), 187(5), 813-818
CODEN: JEMEAV; ISSN: 0022-1007
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human histocompatibility leukocyte antigen (**HLA**)-**E** is a nonclassical HLA class I mol., the gene for which is transcribed in most tissues. It has recently been reported that this mol. binds peptides derived from the signal sequence of HLA class I proteins; however, no function for **HLA**-**E** has yet been described. The authors show that natural killer (**NK**) cells can recognize target cells expressing **HLA**-**E** mols. on the cell surface and this interaction results in inhibition of the lytic process. Furthermore, **HLA**-**E** recognition is mediated primarily through the **CD94/NKG2**-A heterodimer, as **CD94**-specific, but not killer cell inhibitory receptor (KIR)-specific mAbs block **HLA**-**E**-mediated protection of target cells. Cell surface **HLA**-**E** could be increased by incubation with synthetic peptides corresponding to residues 3-11 from the signal sequences of a no. of HLA class I mols.; however, only peptides which contained a Met at position 2 were capable of conferring resistance to **NK**-mediated lysis, whereas those having Thr at position 2 had no effect. Interestingly, HLA class I mols. previously correlated with **CD94/NKG2** recognition all have Met at residue 4 of the signal sequence (position 2 of the **HLA**-**E** binding peptide), whereas those which have been reported not to interact with **CD94/NKG2** have Thr at this position. These data thus show a function for **HLA**-**E** and suggest an alternative explanation for the apparent broad reactivity of **CD94/NKG2** with HLA class I mols.; that **CD94/NKG2** interacts with **HLA**-**E** complexed with signal sequence peptides derived from "protective" HLA class I alleles rather than directly interacting with classical HLA class I proteins.

L8 ANSWER 8 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 7
ACCESSION NUMBER: 1998:134074 CAPLUS
DOCUMENT NUMBER: 128:269312
TITLE: **HLA**-**E** binds to natural killer cell receptors **CD94/NKG2A**, B and C
AUTHOR(S): Braud, Veronique M.; Allan, David S. J.; O'Callaghan, Christopher A.; Soderstrom, Kalle; D'Andrea, Annalisa; Ogg, Graham S.; Lazatic, Sasha; Young, Neil T.; Bell, John I.; Phillips, Joseph H.; Lanier, Lewis L.; McMichael, Andrew J.
CORPORATE SOURCE: Inst. Molecular Med., John Radcliffe Hosp., Oxford, OX3 9DS, UK
SOURCE: Nature (London) (**1998**), 391(6669), 795-799
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Macmillan Magazines
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The protein **HLA**-**E** is a non-classical major histocompatibility complex (MHC) mol. of limited sequence variability. Its expression on the cell surface is regulated by the binding of peptides derived from the signal sequence of some other MHC class I mols. Here we report the identification of ligands for **HLA**-**E**. We constructed tetramers in which recombinant **HLA**-**E** and .beta.2-microglobulin were refolded with an MHC, leader-sequence peptide, biotinylated, and conjugated to phycoerythrin-labeled Extravidin. This **HLA**-**E** tetramer bound to natural killer (**NK**) cells and a small subset of T cells from peripheral blood. On transfectants, the tetramer bound to the **CD94/NKG2A**, **CD94/NKGK2B** and **CD94/NKG2C** NM cell receptors, but did not bind to the Ig family of **NK** cell receptors (KIR). Surface expression of **HLA**-**E** was enough to protect target cells from lysis by **CD94/NKG2A** + **NK**-cell clones. A subset of HLA class I alleles has been shown to inhibit killing by **CD94/NKG2A**+ **NK** -cell clones. Only the HLA alleles that posses a leader peptide capable of upregulating **HLA**-**E** surface expression confer resistance to **NK**-cell-mediated lysis, implying that their action is mediated by **HLA**-**E**, the predominant ligand for the **NK** cell inhibitory receptor **CD94/NKG2A**.

L8 ANSWER 9 OF 30 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:226619 CAPLUS
DOCUMENT NUMBER: 128:320229
TITLE: Follow the leader: NK cell receptors for classical and nonclassical MHC class I
AUTHOR(S): Lanier, Lewis L.
CORPORATE SOURCE: Immunobiology Department, DNAX Research Institute of Molecular and Cellular Biology, Palo Alto, CA, 94304, USA
SOURCE: Cell (Cambridge, Massachusetts) (**1998**), 92(6), 705-707
CODEN: CELLB5; ISSN: 0092-8674
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 15 refs., discussing the function of mouse Ly49 receptors, the structure and function of human KIR receptors, and the mol.

interaction of **HLA-E** with **CD94/NKG2** heterodimers.

L8 ANSWER 10 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 8
ACCESSION NUMBER: 1998:417529 CAPLUS
DOCUMENT NUMBER: 129:160384
TITLE: Association of DAP12 with activating CD94/NKG2C NK cell receptors
AUTHOR(S): Lanier, Lewis L.; Corliss, Brian; Wu, Jun; Phillips, Joseph H.
CORPORATE SOURCE: Immunobiology Dept., DNAX Research Inst. of Molecular and Cellular Biology, Palo Alto, CA, 94304, USA
SOURCE: Immunity (1998), 8(6), 693-701
CODEN: IUNIEH; ISSN: 1074-7613
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB While the inhibitory **NK** cell receptors for MHC class I express immunoreceptor tyrosine-based inhibitory motifs that recruit intracellular tyrosine phosphatases and prevent **NK** cell effector function, the activating **NK** cell receptors lack intrinsic sequences required for cellular stimulation. **CD94/NKG2C**, an activating **NK** cell receptor of the C-type lectin superfamily that binds to **HLA-E**, noncovalently assocs. with DAP12, a membrane receptor contg. an immunoreceptor tyrosine-based activating motif. Efficient expression of **CD94/NKG2C** on the cell surface requires the presence of DAP12, and charged residues in the transmembrane domains of DAP12 and **NKG2C** are necessary for this interaction. These results provide a mol. basis for the assembly of **NK** cell receptors for MHC class I involved in cellular activation and inhibition.

L8 ANSWER 11 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 9
ACCESSION NUMBER: 1998:225128 CAPLUS
DOCUMENT NUMBER: 129:3675
TITLE: Structural features impose tight peptide binding specificity in the nonclassical MHC molecule HLA-E
AUTHOR(S): O'callaghan, Christopher A.; Tormo, Jose; Willcox, Benjamin E.; Braud, Veronique M.; Jakobsen, Bent K.; Stuart, David I.; Mcmichael, Andrew J.; Bell, John I.; Jones, E. Yvonne
CORPORATE SOURCE: Molecular Immunology Group, Nuffield Department of Clinical Medicine, Institute of Molecular Medicine, John Radcliffe Hospital, University of Oxford, Oxford, OX3 9DS, UK
SOURCE: Molecular Cell (1998), 1(4), 531-541
CODEN: MOCEFL; ISSN: 1097-2765
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The crystal structure of the nonclassical human class Ib MHC mol. **HLA-E** has been detd. in complex with a prototypic ligand, the nonamer peptide (VMAPRTVLL), derived from the highly conserved residues 3-11 of the human MHC class Ia leader sequence. The mode of peptide binding retains some of the std. features obsd. in MHC class Ia complexes, but novel features imply that **HLA-E** has evolved to mediate specific binding to a tightly defined set of almost identical hydrophobic peptides from the highly conserved class I leader sequences. These mol. adaptations make **HLA-E** a rigorous checkpoint at the cell surface reporting on the integrity of the antigen processing pathway to **CD94/NKG2** receptor-bearing natural killer cells.

L8 ANSWER 12 OF 30 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:179237 CAPLUS
DOCUMENT NUMBER: 131:17585
TITLE: Human C-type lectin receptors involved in NK cell mediated recognition of HLA class I molecules
AUTHOR(S): Bellon, Teresa; Navarro, Francisco; Llano, Manuel; Garcia, Pilar; Lopez-Botet, Miguel
CORPORATE SOURCE: Servicio de Immunologia, Hospital Universitario de la Princesa, Madrid, 28006, Spain
SOURCE: Periodicum Biologorum (1998), 100(4), 441-443
CODEN: PDBIAD; ISSN: 0031-5362
PUBLISHER: Hrvatsko Prirodoslovno Drustvo
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 42 refs. discussing the function of CD94/NKG2 heterodimers and their ligand specificity.
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 10
ACCESSION NUMBER: 1998:685732 CAPLUS
DOCUMENT NUMBER: 129:288814
TITLE: **HLA-E** is the ligand for the natural killer cell **CD94/NKG2** receptors
AUTHOR(S): Posch, Phillip E.; Borrego, Francisco; Brooks, Andrew G.; Coligan, John E.
CORPORATE SOURCE: Structural Biology Section, National Inst. Allergy Infectious Disease, National Inst. Health, Rockville, MD, 20852, USA
SOURCE: Journal of Biomedical Science (Basel) (1998), 5(5), 321-331
CODEN: JBCIEA; ISSN: 1021-7770
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review is given with 102 refs. **CD94/NKG2** is a recently described receptor present on natural killer (**NK**) cells and certain T cells that is composed of the **CD94** chain covalently assocd. with a member of the **NKG2** family of mols. Both chains are glycosylated members of the C-type lectin superfamily. The **CD94/NKG2** receptors are functionally heterogeneous depending on which **NKG2** family member is assocd. with **CD94**. It was thought that **CD94/NKG2** receptors recognized a broad array of HLA-A, -B, and -C (classical), as well as the nonclassical HLA-G, MHC class I mols. Recent data have suggested that this receptor is specific for **HLA-E** complexed with a peptide derived from the signal sequence (residues 3-11) of certain classical MHC class I mols. Position 2 (residue 4) in the signal sequence

derived peptides appears pivotal in detg. whether the **HLA-E**/peptide complex confers resistance to **NK**-mediated lysis. The potential roles that the **CD94/NKG2-HLA-E** receptor ligand interaction might play in infection and tumor development are discussed.

L8 ANSWER 14 OF 30 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:676185 CAPLUS
DOCUMENT NUMBER: 130:36956
TITLE: Cytotoxic lymphocyte recognition of HLA-E: utilizing a nonclassical window to peer into classical MHC
AUTHOR(S): Leibson, Paul J.
CORPORATE SOURCE: Department of Immunology, Mayo Clinic and Foundation, Rochester, MN, 55905, USA
SOURCE: Immunity (**1998**), 9(3), 289-294
CODEN: IUNIEH; ISSN: 1074-7613
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 50 refs. This paper discusses how recognition of **HLA-E** enables **NK** cells to monitor the integrity of the MHC class I-dependent antigen presentation pathway. Since certain subpopulations of activated cytotoxic T cells (CTLs) can also express the **HLA-E**-recognizing inhibitory receptors, exptl. results are described regarding the effects of inhibitory receptors on CTL activation. Finally, the potential implications of **HLA-E** recognition on antitumor immunity, antiviral immunity, and materno-fetal interactions are discussed.
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 15 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 11
ACCESSION NUMBER: 1998:543874 CAPLUS
DOCUMENT NUMBER: 129:274318
TITLE: Structure and function of the human MHC class Ib molecules HLA-E, HLA-F and HLA-G
AUTHOR(S): O'Callaghan, Christopher A.; Bell, John I.
CORPORATE SOURCE: Molecular Immunology Group, Nuffield Department Clinical Medicine, Institue Molecular Medicine, John Radcliffe Hospital, University Oxford, Oxford, UK
SOURCE: Immunological Reviews (**1998**), 163, 129-138
CODEN: IMRED2; ISSN: 0105-2896
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 49 refs. The major histocompatibility (MHC) class Ib mols. **HLA-E**, **HLA**-F and HLA-G are relatively non-polymorphic compared to class Ia mols. Both **HLA-E** and **HLA**-G bind peptides and are involved in natural killer (**NK**)-cell recognition, but the role of HLA-F is unclear. **HLA-E** binds specifically to the conserved leader sequence peptides from the class Ia MHC mols. and interacts on the cell surface with the **CD94/NKG2** class of **NK**-cell receptors. The framework structure of **HLA-E** is similar to that of the MHC class Ia mols., but the peptide-binding groove is highly adapted for the specific binding of the leader sequence peptides. This is different from class Ia mols., which have highly promiscuous peptide-binding grooves. The **HLA-E** groove makes full use of all the available pockets and imposes specificity along the entire length of the peptide. HLA-G binds nonamer peptides with leucine or isoleucine at position 2, proline at position 3 and leucine at position 9. Expression of HLA-G inhibits **NK** cells expressing the **CD94/NKG2** class of receptors, though an interaction with these receptors has not been directly demonstrated.

L8 ANSWER 16 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:219822 BIOSIS
DOCUMENT NUMBER: PREV199900219822
TITLE: **HLA-E**-bound peptides influence recognition by inhibitory and triggering **CD94/NKG2** receptors: Preferential response to an HLA-G-derived nonamer.
AUTHOR(S): Llano, Manuel (1); Lee, Ni; Navarro, Francisco (1); Garcia, Pilar (1); Albar, Juan Pablo; Geraghty, Daniel E.; Lopez-Botet, Miguel (1)
CORPORATE SOURCE: (1) Hospital Universitario de la Princesa, Madrid Spain
SOURCE: Natural Immunity, (**Feb., 1998**) Vol. 16, No. 2-3, pp. 80.
Meeting Info.: Fifth Annual Meeting of the Society for Natural Immunity Seventeenth International Natural Killer Cell Workshop Warrenton, Virginia, USA October 17-21, 1998
ISSN: 1018-8916.
DOCUMENT TYPE: Conference
LANGUAGE: English

L8 ANSWER 17 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:219821 BIOSIS
DOCUMENT NUMBER: PREV199900219821
TITLE: Decidual **NK** cells have receptors for **HLA-E** which is expressed by human trophoblast.
AUTHOR(S): Allan, D.S.J. (1); Verma, S.; Bowen, J. M.; Loke, Y. W.; McMichael, J. (1); Braud, V. M. (1); King, A.
CORPORATE SOURCE: (1) Institute of Molecular Medicine, John Radcliffe Hospital, Oxford, OX3 9DS UK
SOURCE: Natural Immunity, (**Feb., 1998**) Vol. 16, No. 2-3, pp. 79.
Meeting Info.: Fifth Annual Meeting of the Society for Natural Immunity Seventeenth International Natural Killer Cell Workshop Warrenton, Virginia, USA October 17-21, 1998
ISSN: 1018-8916.
DOCUMENT TYPE: Conference
LANGUAGE: English

L8 ANSWER 18 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:219811 BIOSIS
DOCUMENT NUMBER: PREV199900219811
TITLE: Specific recognition of **HLA-E** but not classical HLA class I molecules by soluble **CD94/NKG2A** and **NK** cells.
AUTHOR(S): Brooks, Andrew G. (1); Borrego, Francisco; Posch, Phillip E. (1); Patamawenu, Apisit (1); Coligan, John E.

CORPORATE SOURCE: (1) Structural Biology Section, National Institute of Allergy and Infectious Disease, National Institutes of Health, Twinbrook II, Rockville, MD, 20852 USA
SOURCE: Natural Immunity, (**Feb., 1998**) Vol. 16, No. 2-3, pp. 72.
Meeting Info.: Fifth Annual Meeting of the Society for Natural Immunity Seventeenth International Natural Killer Cell Workshop Warrenton, Virginia, USA October 17-21, 1998
ISSN: 1018-8916.
DOCUMENT TYPE: Conference
LANGUAGE: English

L8 ANSWER 19 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:219810 BIOSIS
DOCUMENT NUMBER: PREV199900219810
TITLE: **NK** cell-mediated recognition of **HLA-E** and **HLA**-G class Ib molecules.
AUTHOR(S): Lopez-Botet, M. (1); Llano, M. (1); Navarro, F. (1); Garcia, P. (1)
CORPORATE SOURCE: (1) S. de Immunologia, Hospital Universitario de la Princesa, 28006, Madrid Spain
SOURCE: Natural Immunity, (**Feb., 1998**) Vol. 16, No. 2-3, pp. 71.
Meeting Info.: Fifth Annual Meeting of the Society for Natural Immunity Seventeenth International Natural Killer Cell Workshop Warrenton, Virginia, USA October 17-21, 1998
ISSN: 1018-8916.
DOCUMENT TYPE: Conference
LANGUAGE: English

L8 ANSWER 20 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 12
ACCESSION NUMBER: 1998:23376 CAPLUS
DOCUMENT NUMBER: 128:137001
TITLE: Mhc-E polymorphism in Pongidae primates: the same allele is found in two different species
AUTHOR(S): Suarez, B.; Morales, P.; Castro, M. J.; Fernandez-Soria, V.; Recio, M. J.; Perez-Blas, M.; Alvarez, M.; Diaz-Campos, N.; Arnaiz-Villena, A.
CORPORATE SOURCE: Department of Immunology, Hospital 12 de Octubre, Universidad Complutense, Madrid, Spain
SOURCE: Tissue Antigens (**1997**), 50(6), 695-698
CODEN: TSANA2; ISSN: 0001-2815
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mhc-E intron 1, exon 2, intron 2, and exon 3 from pygmy chimpanzee (Pan paniscus), chimpanzee (Pan troglodytes), gorilla (Gorilla gorilla) and orangutan (Pongo pygmaeus) have been sequenced; six new Mhc-E alleles have been obtained but sequence changes are only placed either in introns or in synonymous exonic bases. One pygmy chimpanzee Mhc-E DNA sequence is identical to another sequence from chimpanzee; the fact that no variation is found also at the intronic level suggests that these two species of chimpanzee may have recently sepd. and/or that both of them might only represent subspecies. Mhc-E phylogenetic trees sep. two evolutionary groups: Pongidae, including humans, and Cercopithecinae; this is also found by studying another non-classical class I gene, Mhc-G. The Mhc-E alleles' invariance at the protein level supports that strong selective forces are operating at the Mhc-E locus, as has also been found in both Cercopithecinae and humans. These allelic and evolutionary data suggest an altogether different functionality for **HLA-E** (and also HLA-G) compared with classical class I proteins: i.e., sending neg. (tolerogenic) signals to **NK** and T cells.

L8 ANSWER 21 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 13
ACCESSION NUMBER: 1997:111333 CAPLUS
DOCUMENT NUMBER: 126:184797
TITLE: Human histocompatibility leukocyte antigen (HLA)-G molecules inhibit NKAT3 expressing natural killer cells
AUTHOR(S): Muenz, Christian; Holmes, Nicholas; King, Ashley; Loke, Yung Wai; Colonna, Marco; Schild, Hansjoerg; Rammensee, Hans-Georg
CORPORATE SOURCE: Dep. Immunology, Univ. Tuebingen, Tuebingen, 72076, Germany
SOURCE: Journal of Experimental Medicine (**1997**), 185(3), 385-391
CODEN: JEMEAV; ISSN: 0022-1007
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The crucial immunol. function of the classical human major histocompatibility complex (MHC) class I mols., human histocompatibility leukocyte antigen (HLA)-A, -B, and -C, is the presentation of peptides to T cells. A second function is the inhibition of natural killer (**NK**) cells, mediated by binding of class I mols. to **NK** receptors. In contrast, the function of the nonclassical human MHC class I mols., **HLA-E**, -F, and -G, is still a mystery. The specific expression of HLA-G in placental trophoblast suggests an important role for this mol. in the immunol. interaction between mother and child. Ths fetus, semiallograft by its genotype, escapes maternal allorecognition by downregulation of HLA-A and HLA-B mols. at this interface. It has been suggested that the maternal **NK** recognition of this downregulation is balanced by the expression of HLA-G, thus preventing damage to the placenta. Here, we describe the partial inhibition of **NK** lysis of the MHC class I neg. cell line LCL721.221 upon HLA-G transfection. We present three **NK** lines that are inhibited via the interaction of their **NKAT3** receptor with HLA-G and with HLA-Bw4 mols. Inhibition can be blocked by the anti-**NKAT3** antibody 5.133. In conclusion, **NK** inhibition by HLA-G via **NKAT3** may contribute to the survival of the fetal semiallograft in the mother during pregnancy.

L8 ANSWER 22 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:227193 BIOSIS
DOCUMENT NUMBER: PREV199799518909
TITLE: The Thomas G. Wegmann Memorial Symposium on reproductive immunology: Banff, Alberta, Canada, (September 12, 1996.
AUTHOR(S): Vince, G.
CORPORATE SOURCE: Dep. Immunol., Univ. Liverpool, Duncan Build., Liverpool L69 3BX UK
SOURCE: Placenta, (1997) Vol. 18, No. 2-3, pp. 234-235.
ISSN: 0143-4004.

DOCUMENT TYPE: Conference; Report
LANGUAGE: English

L8 ANSWER 23 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 14
ACCESSION NUMBER: 96353415 EMBASE
DOCUMENT NUMBER: 1996353415
TITLE: [The class I region of the MHC genes is one of the most complex in the whole human genome].
LA REGION HLA DE CLASSE I: UNE ORGANISATION COMPLIQUEE PAR LA PRESENCE DE NOMBREUSES FAMILLES MULTIGENIQUES.
AUTHOR: Pichon L.; Giffon T.; Chauvel B.; Le Gall J.-Y.; David V.
CORPORATE SOURCE: UPR Cnrs, Recombinaisons genetiques, Faculte de Medecine, 2 avenue du Pr-Leon Bernard,35043 Rennes Cedex, France
SOURCE: Medecine/Sciences, (1996) 12/11 (1209-1218).
ISSN: 0767-0974 CODEN: MSMSE4
COUNTRY: France
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 022 Human Genetics
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: French
SUMMARY LANGUAGE: French; English
AB The human major histocompatibility complex (MHC) is a 4-Mb genomic segment located on chromosome 6, in the distal portion of the 6p21.3 band. The MHC is a well described region of the human genome and represents a cluster of genes intensively studied because of the important functions of the gene products in the immune system. The total number of genes located within the MHC is now approximately 100, but more can be predicted. The density of genes in the Class II and Class III regions has been known for several years, but the high density of genes in the Class I region did only recently become apparent. This class I region spans 2,000 kb on the telomeric half of the MHC, and contains six class I genes, three of which, the classical human leukocyte antigen genes HLA-A, HLA-B and HLA-C, encode membrane-anchored cell surface glycoproteins that present the endogenous antigenic peptides to the T cell receptors and are recognized by NK cell receptors. These genes are characterized by a high polymorphism and a nearly ubiquitous expression. The biological function of the three nonclassical class I genes HLA-E, HLA-F, and HLA-G still remains uncertain. In addition to these six genes, the MHC contains a number of class I pseudoaenes and gene fragments whose close relationship indicates a common origin from a typical HLA class I ancestor gene. This region appears also to harbour various non-HLA single copy genes such as OTP3, TCF19, S gene, TUBB, HSR1, B30.2, ZNF173, HCG V, HCG-VII, MOG or OLFR2 as well as eight recently described multigene families named P5.1, 3.8-1, PERB11, BAT1, HCGII, HCGIV, HCGVIII and HCGIX containing a number of sequences displayed throughout the HLA Class I region. The presence of all these coding sequences and multigene families suggests that the gene density of the HLA Class I region is comparable to that of the class II and class III regions, i.e. one gene per 20 or 30 kb. We present here a new map compiling the update knowledge of the structure of this Class I region.

L8 ANSWER 24 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 15
ACCESSION NUMBER: 1994:506185 CAPLUS
DOCUMENT NUMBER: 121:106185
TITLE: NKB1: a natural killer cell receptor involved in the recognition of polymorphic HLA-B molecules
AUTHOR(S): Litwin, Virginia; Gumperz, Jenny; Parham, Peter; Phillips, Joseph H.; Lanier, Lewis L.
CORPORATE SOURCE: Department of Human Immunology, DNAX Research Institute of Molecular Cellular Biology, Inc., Palo Alto, CA, 94304, USA
SOURCE: J. Exp. Med. (1994), 180(2), 537-43
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Natural killer (NK) cells kill normal and transformed hematopoietic cells that lack expression of major histocompatibility complex (MHC) class I antigens. Lysis of HLA-neg. Epstein Barr virus-transformed B lymphoblastoid cell lines (B-LCL) by human NK cell clones can be inhibited by transfection of the target cells with certain HLA-A, -B, or -C alleles. NK cell clones established from an individual demonstrate clonal heterogeneity in HLA recognition and a single NK clone can recognize multiple alleles. The authors describe a potential human NK cell receptor (NKB1) for certain HLA-B alleles (e.g., HLA-B*5101 and -B*5801) identified by the mAb DX9. NKB1 is a 70 kDa glycoprotein that is expressed on a subset of NK cells and NK cell clones. DX9 monoclonal antibody (mAb) specifically inhibits the interaction between NK cell clones and B-LCL targets transfected with certain HLA-B alleles, but does not affect recognition of HLA-A or HLA-C antigens. An individual NK cell clone can independently recognize B-LCL targets transfected with HLA-B or HLA-C antigens; however, DX9 mAb only affects interaction with transfectants expressing certain HLA-B alleles. These findings demonstrate the existence of NK cell receptors involved in the recognition of HLA-B and imply the presence of multiple receptors for MHC on an individual NK clone.

L8 ANSWER 25 OF 30 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 16
ACCESSION NUMBER: 1993:20561 CAPLUS
DOCUMENT NUMBER: 118:20561
TITLE: Role for major histocompatibility complex class I in regulating natural killer cell-mediated killing of virus-infected cells
AUTHOR(S): Kaufman, Dan S.; Schoon, Renee A.; Leibson, Paul J.
CORPORATE SOURCE: Dep. Immunol., Mayo Clin. Found., Rochester, MN, 55905, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1992), 89(17), 8337-41
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Target structures important for natural killer (NK) cell recognition of virally infected cells are not well defined. Since major histocompatibility complex (MHC) class I mols. bind viral peptides during acute infection, it was evaluated whether an interaction between MHC and virus might influence the susceptibility of infected cells to NK cell-mediated lysis. To control for MHC class I expression on target cells, either HLA class I-deficient C1R cells or C1R sublines expressing transfected HLA class I gene products were used. Human NK cells were unable to preferentially lyse class I-deficient C1R cells after infection with herpes simplex virus (HSV). In contrast, HLA class I

transfectants were more susceptible to **NK** cell-mediated cytotoxicity after HSV infection. This occurred for HSV-infected C1R cells expressing any of the 3 HLA class I gene products tested (i.e., **HLA**-B27, HLA-A3, or HLA-Aw68), indicating that **NK** cells recognition in this system does not require self MHC and is not unique for a single haplotype. Productive HSV infection is required for the increased killing, since inoculation with UV-inactivated virus did not lead to increased lysis. In addn., since HSV infection of the transfectants did not alter the level of class I expression, the change in susceptibility appears to be due to qual. changes in the target structures on HSV-infected, HLA class I+ targets. These results demonstrate a role for MHC class I in regulating **NK** cell-mediated killing of virus-infected cells.

L8 ANSWER 26 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 17
ACCESSION NUMBER: 92041666 EMBASE
DOCUMENT NUMBER: 1992041666
TITLE: Cloning and expression of a cDNA encoding a non-classical MHC class I antigen (HLA-E) in eosinophils from hypereosinophilic patients.
AUTHOR: Truong M.-J.; Gruart V.; Capron A.; Capron M.; Tourvieille B.
CORPORATE SOURCE: Ctr. d'Immunol. Biol. Parasit., INSERM U167-CNRS 624, Institut Pasteur, 1 Rue du Pr. Calmette,59019 Lille Cedex, France
SOURCE: Journal of Immunology, (**1992**) 148/2 (627-632).
ISSN: 0022-1767 CODEN: JOIMA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
025 Hematology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A cDNA library, constructed from purified blood eosinophils, was screened with the B cell CD23 cDNA probe. A clone designated EO15 has been isolated and found to encode a non-classical HLA class I gene transcript. EO15 was compared with **HLA**-**E** and found to be 99.9% similar at the nucleotide level and to extend further in the 3' untranslated region. The presence of an additional polyadenylation signal in the EO15 3' end suggests that EO15 clone represents a copy of the 3.3-kb mRNA species detected in Northern blot analyses. **HLA**-**E** transcripts of 1.9 and 3.3 kb have been described in a variety of cell types. The two EO15 mRNA species, similar in size to the previously defined **HLA**-**E** mRNA, were present at high levels in blood leukocyte populations and at variable levels in different cell lines. The EO15 transcripts were found at abundant levels in hypodense and normodense eosinophils from hypereosinophilic patients. In situ hybridization confirmed the expression of EO15 mRNA in eosinophils. Neutrophils and lymphocytes from normal donors or from patients with hypereosinophilia also strongly expressed EO15 mRNA. Among the cell lines studied, the highest levels of EO15 transcripts were detected in B and monocytic cell lines, whereas intermediate and lower levels were found in eosinophilic, **NK**-like, megakaryocytic, and T cell lines, respectively. Similar to its effect on classical HLA class I transcripts, IFN-.gamma. increased the levels of EO15 mRNA in eosinophils and neutrophils from hypereosinophilic patients. These results suggest that purified blood eosinophils as well as neutrophils express EO15/**HLA**-**E** mRNA; however, further experiments are needed to investigate the localization and the function of EO15 protein products.

L8 ANSWER 27 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93075714 EMBASE
DOCUMENT NUMBER: 1993075714
TITLE: Recent advances in human natural killer cells.
AUTHOR: Moretta L.; Ciccone E.; Biassoni R.; Poggi A.; Mingari M.C.; Moretta A.
CORPORATE SOURCE: Isto Naz per la Ricerca sul Cancro, Viale Benedetto XV,10 1-16132 Genova, Italy
SOURCE: International Archives of Allergy and Immunology, (**1992**) 99/2-4 (230-233).
ISSN: 1018-2438 CODEN: IAAIEG
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 016 Cancer
025 Hematology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB This paper reviews recent progresses on human Natural Killer (**NK**) cells which profoundly changed our concepts on **NK** cells and their functions. Regarding the ontogeny of **NK** cells, immature thymocyte populations (CD-3-4-16-) have been shown to give rise to **NK** cells, provided suitable culture conditions. This indicates that precursor potentially capable of differentiation towards the **NK** cell lineage are present within the human thymus. Although **NK** cells lack known receptors for antigen (i.e. sIg and TCR), **NK** cell populations or clones were found to be capable of mediating specific recognition of allogenic cells. This specific function was clonally distributed and, more importantly, **NK** clones displaying different patterns of allospecificity could be isolated from single individuals. These data indicate the existence of a **NK** cell repertoire for alloantigen recognition. Analysis of the surface molecules identified by **NK** cells indicated that certain **HLA** alleles (e.g. **HLA**-Cw3) can act as specific protective elements from lysis by clones with defined specificities (e.g. specificity 2). Therefore, HLA class I molecules appear to play a central role in the **NK** cell-mediated functions. The finding that human **NK** cells express a clonally-dystributed ability to recognize alloantigens suggested the existence of distinct surface receptors. Indeed, a new family of triggering surface molecules (58 kD) has been identified by the use of monoclonal antibodies. The expression of these molecules was shown to represent a stable phenotipic property of human **NK** cells and to be clonally distributed. More importantly, the expression of 58 kD molecules appears to correlate with the ability to recognize given allospecificities. These data are supporting the concept that 58 kD molecules are part of receptor structures involved in the **NK** cell-mediated recognition.

L8 ANSWER 28 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 18
ACCESSION NUMBER: 90120495 EMBASE
DOCUMENT NUMBER: 1990120495

TITLE: Dendritic cells stimulate primary human cytolytic lymphocyte responses in the absence of CD4+ helper T cells.
AUTHOR: Young J.W.; Steinman R.M.
CORPORATE SOURCE: The Rockefeller University, Box 280, 1230 York Avenue,New York, NY 10021, United States
SOURCE: Journal of Experimental Medicine, (1990) 171/4 (1315-1332).
ISSN: 0022-1007 CODEN: JEMEAV
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 025 Hematology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Cytotoxic lymphocytes are typically generated from unfractionated suspensions of human lymphocytes by stimulating with heterogeneous APCs and exogeneous growth factors. We have found that human blood dendritic cells can directly stimulate allogeneic human CD8+ T cells to proliferate and express antigen-specific cytotoxic activity. These primary responses, which are accompanied by the release of T cell growth factor(s), are induced in the absence of CD4+ helper T cells and are not inhibited by anti-CD4 mAb. Both antigen-specific CTL as well as nonspecific **NK** cells can be elicited by dendritic cells. The **NK** cell response can be depleted at the precursor level by panning with an anti-CD11b mAb, which removes a CD11b+/CD28-, CD16+ subset from the starting CD4- responders. Allogeneic blood monocytes are neither stimulatory nor inhibitory of these primary CD4- MLRs, even though monocytes present alloantigen in such a way as to be recognized as specific targets for CTL that have been sensitized by dendritic cells. The number of CD8+ cells that are blast transformed and express an activated phenotype (i.e., **HLA** DR/DQ+, CD25/IL-2R+, CD45R-) reaches 30-40% of the culture at day 4-5, the peak of the helper-independent response. We conclude that antigen-presentation by dendritic cells is sufficient in itself to prime cytolytic precursors. We speculate that using dendritic cell stimulators and CD4- responders in MLRs may be more efficient than standard tissue typing approaches for the detection of subtle, but important class I MHC-restricted histoincompatibilities in human transplantation.

L8 ANSWER 29 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 19
ACCESSION NUMBER: 89048435 EMBASE
DOCUMENT NUMBER: 1989048435
TITLE: Use of anti-HLA antibodies to mask major histocompatibility complex gene products on tumor cells can enhance susceptibility of these cells to lysis by natural killer cells.
AUTHOR: Lobo P.I.; Spencer C.E.
CORPORATE SOURCE: Department of Medicine, University of Virginia School of Medicine, Charlottesville, VA 22908, United States
SOURCE: Journal of Clinical Investigation, (1989) 83/1 (278-287).
ISSN: 0021-9738 CODEN: JCINAO
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 016 Cancer
022 Human Genetics
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The role of major histocompatibility gene products (i.e., **HLA** molecules) in rendering tumor cells resistant to natural killer (**NK**) cell-mediated lysis was investigated by using mouse monoclonal antibodies to bind and mask HLA or non-HLA gene products on the cell membrane of human allogeneic tumor targets. Enhanced lysis of resistant lymphoid and certain other solid tumor cell lines was observed only when monoclonals used reacted to class I and II HLA molecules but not non-HLA molecules on tumor targets. Enhanced lysis was not due to antibody dependent cellular cytotoxicity or due to an effect of antibody on **NK** effectors. Of importance, normal autologous and allogeneic human lymphocytes could not be lysed by **NK** cells despite blast transformation with mitogens or masking of HLA membrane determinants on blasts with monoclonal antibodies. Enhanced lysis, in the presence of antibody to HLA antigens, was not due to increased **NK** cell binding to tumor targets, but a consequence of enhanced postbinding lysis. Studies using granules obtained from **NK** cells indicated that masking of HLA antigens did not enhance the susceptibility of tumor targets to cytolysis. Such observations would suggest that HLA antigens on tumor targets inhibit the triggering of effector cells (and release of cytolysins) after recognition and binding of **NK** cells to target cells.

L8 ANSWER 30 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 20
ACCESSION NUMBER: 88000518 EMBASE
DOCUMENT NUMBER: 1988000518
TITLE: [Bronchioloalveolar lavage in conjunction with transbronchial lung biopsy: Value and indications]. AUSSAGE- UND EINSATZMOGLICHKEITEN DER BRONCHIOLOALVEOLAREN LAVAGE KOMBINIERT MIT TRANSBRONCHIALER LUNGENBIOPSIE.
AUTHOR: Popper H.; Pongratz M.
CORPORATE SOURCE: Laboratorium fur Umwelt- und Atemtraktpathologie, Institut fur Pathologische Anatomie, Universitat Graz, 8036 Graz, Austria
SOURCE: Wiener Klinische Wochenschrift, (1987) 99/24 (848-855).
ISSN: 0043-5325 CODEN: WKWOAO
COUNTRY: Austria
DOCUMENT TYPE: Journal
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
015 Chest Diseases, Thoracic Surgery and Tuberculosis
LANGUAGE: German
SUMMARY LANGUAGE: English

AB Bronchioloalveolar lavage (BAL) enables diffuse interstitial lung disease to be divided into lymphocytic and granulocytic alveolitis. The combination of BAL and transbronchial lung biopsies using modern flexible fiberoptic bronchoscopes allows the subdivision of lymphocytic alveolitis into sarcoidosis, exogenic allergic alveolitis (synonym: hypersensitivity pneumonitis: EAA) and granulomatous pneumonias caused by infectious agents. The use of immunohistochemical surface markers of lymphocytes in conjunction with BAL provides further differentiation of lymphocytes into T- and B-, T-helper and T-suppressor types, natural killer cells (**NK** cells) and cytotoxic T-cells. A predominance of T-suppressor lymphocytes is an indication of EAA, whereas a predominance of T-helper

lymphocytes is positively correlated with sarcoidosis. Other markers, e.g. HLA-DR, when expressed on the surface of alveolar macrophages, merely indicate activation unrelated to a specific type of lymphocytic alveolitis. BAL is also a new and promising diagnostic tool for pneumoconioses and other types of lung disease caused by inhaled industrial pollutants. Ferruginous bodies and silica crystals, free or ingested by alveolar macrophages, can be found more easily than by scraping tissue blocks or from multiple sections of transbronchial biopsies. BAL cells can easily be processed for electron microscopy and inhaled foreign material can be analysed in an electron microscope using X-ray diffraction analysis (EDAX) or electron spectroscopic imaging (ESI). BAL is also of value in the diagnosis of peripheral lung carcinomas, in addition to cytologic sputum analysis, brush smears, transthoracic fine needle aspiration and transbronchial biopsies. BAL is a valuable diagnostic tool in cases of unusual pneumonia where fungi can be visualized by silver impregnation techniques and viruses by antibodies using immunofluorescence microscopy.

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(FILE 'HOME' ENTERED AT 13:53:22 ON 24 JUN 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 13:53:34 ON 24 JUN 2002

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L1          3511 S BRAUD V?/AU OR ALLAN D?/AU OR OGG G?/AU OR OCALLAGHAN C?/AU O
L2            47 S L1 AND (NK?)
L3            35 S L2 AND (HLA (1N) E)
L4            14 DUP REM L3 (21 DUPLICATES REMOVED)
L5         72958 S NK (P) (NK? OR CD94?)
L6           315 S (HLA (1N) E) (P) (NK? OR CD94?)
L7            63 S L6 AND PD<19981204
L8            30 DUP REM L7 (33 DUPLICATES REMOVED)
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(FILE 'HOME' ENTERED AT 13:53:22 ON 24 JUN 2

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 13:53:34 ON 24 JUN 2002

L1 3511 S BRAUD V?/AU OR ALLAN D?/AU OR OGG G?/AU OR OCALLAGHAN C?/AU O
L2 47 S L1 AND (NK?)
L3 35 S L2 AND (HLA (1N) E)
L4 14 DUP REM L3 (21 DUPLICATES REMOVED)
L5 72958 S NK (P) (NK? OR CD94?)
L6 315 S (HLA (1N) E) (P) (NK? OR CD94?)
L7 63 S L6 AND PD<19981204
L8 30 DUP REM L7 (33 DUPLICATES REMOVED)